FIGURE 1A

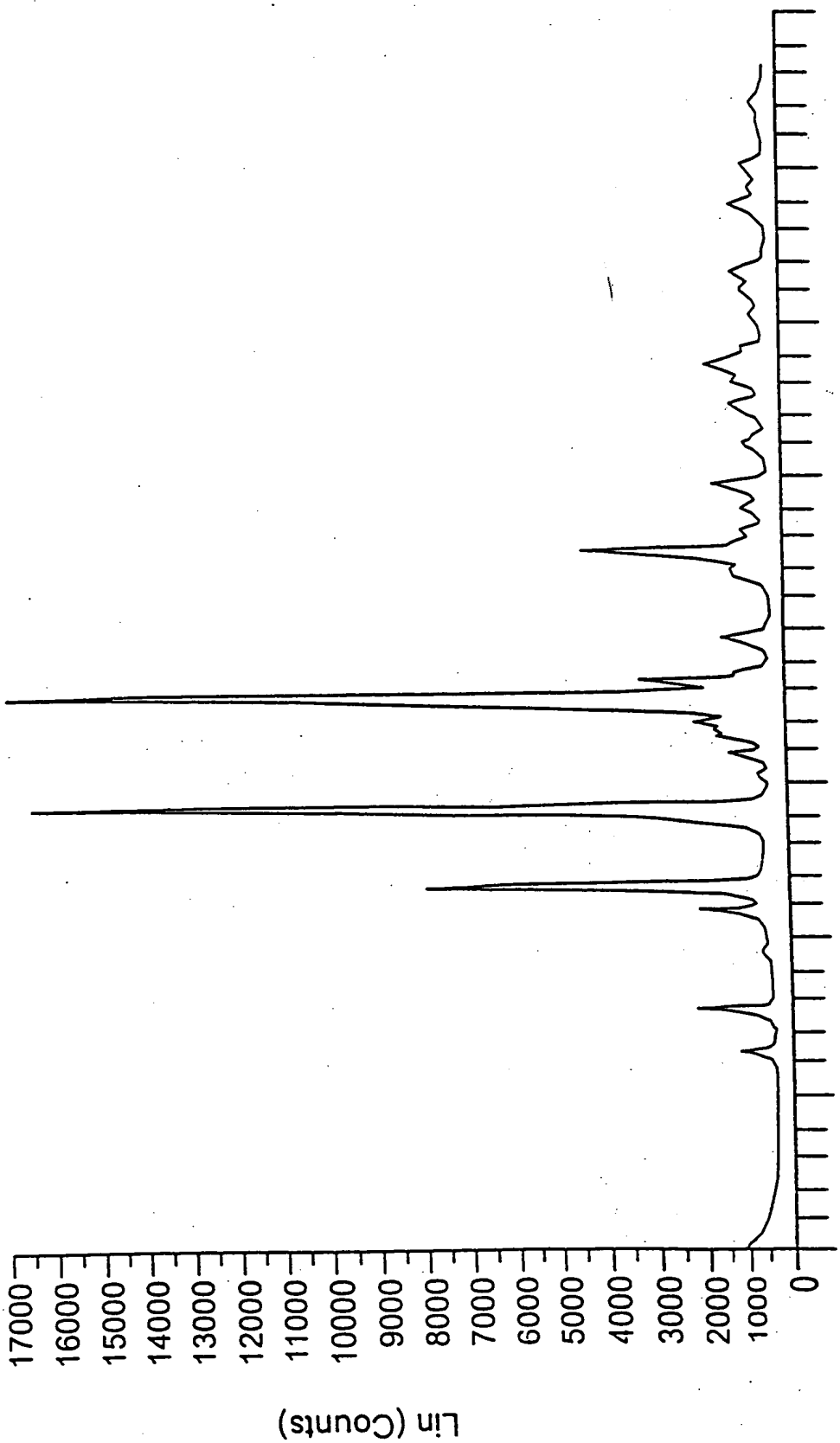

Lin (Counts)
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
2
10
20
30
2-Theta - Scale

FIGURE 1B

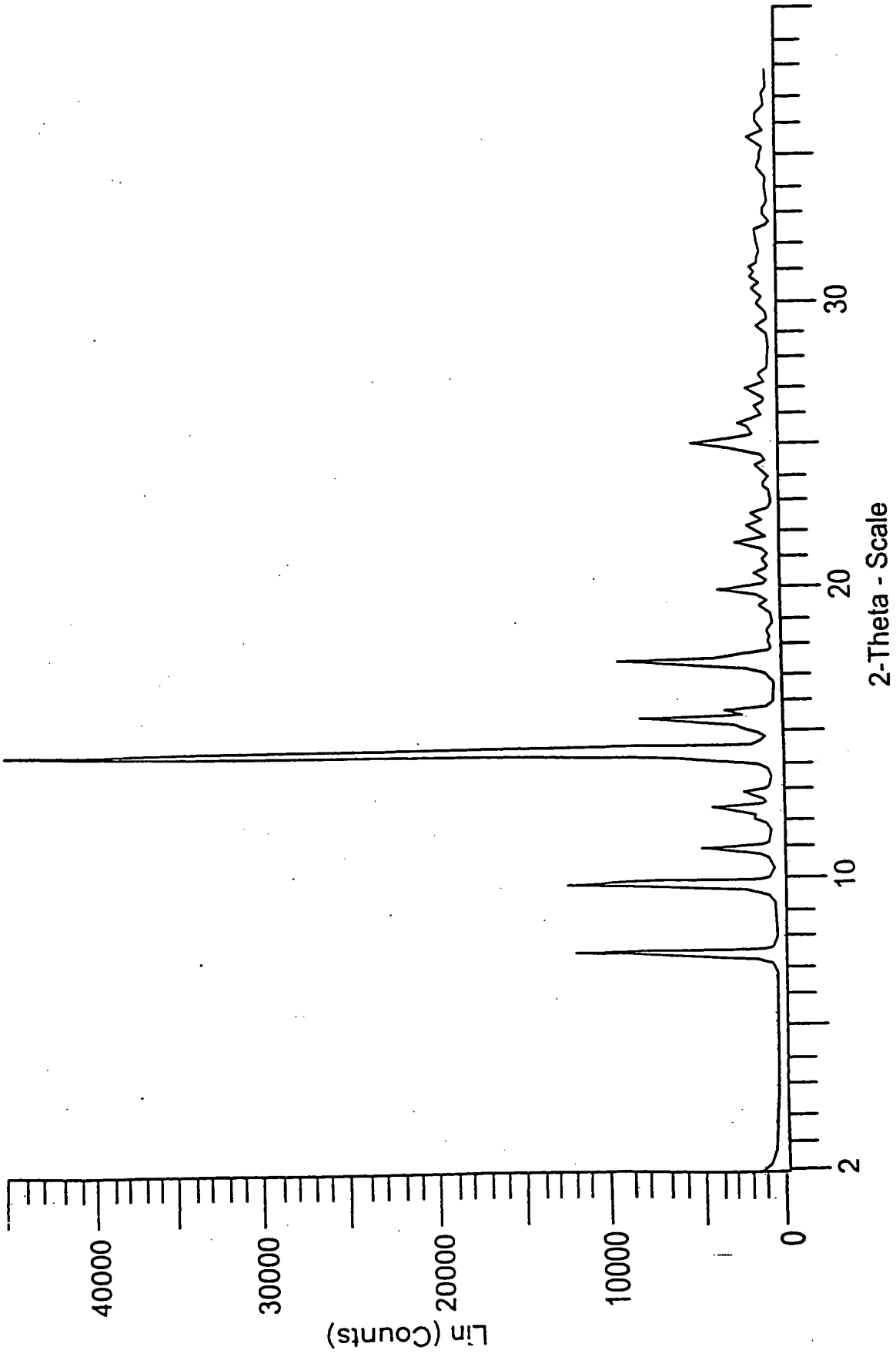


FIGURE 1C

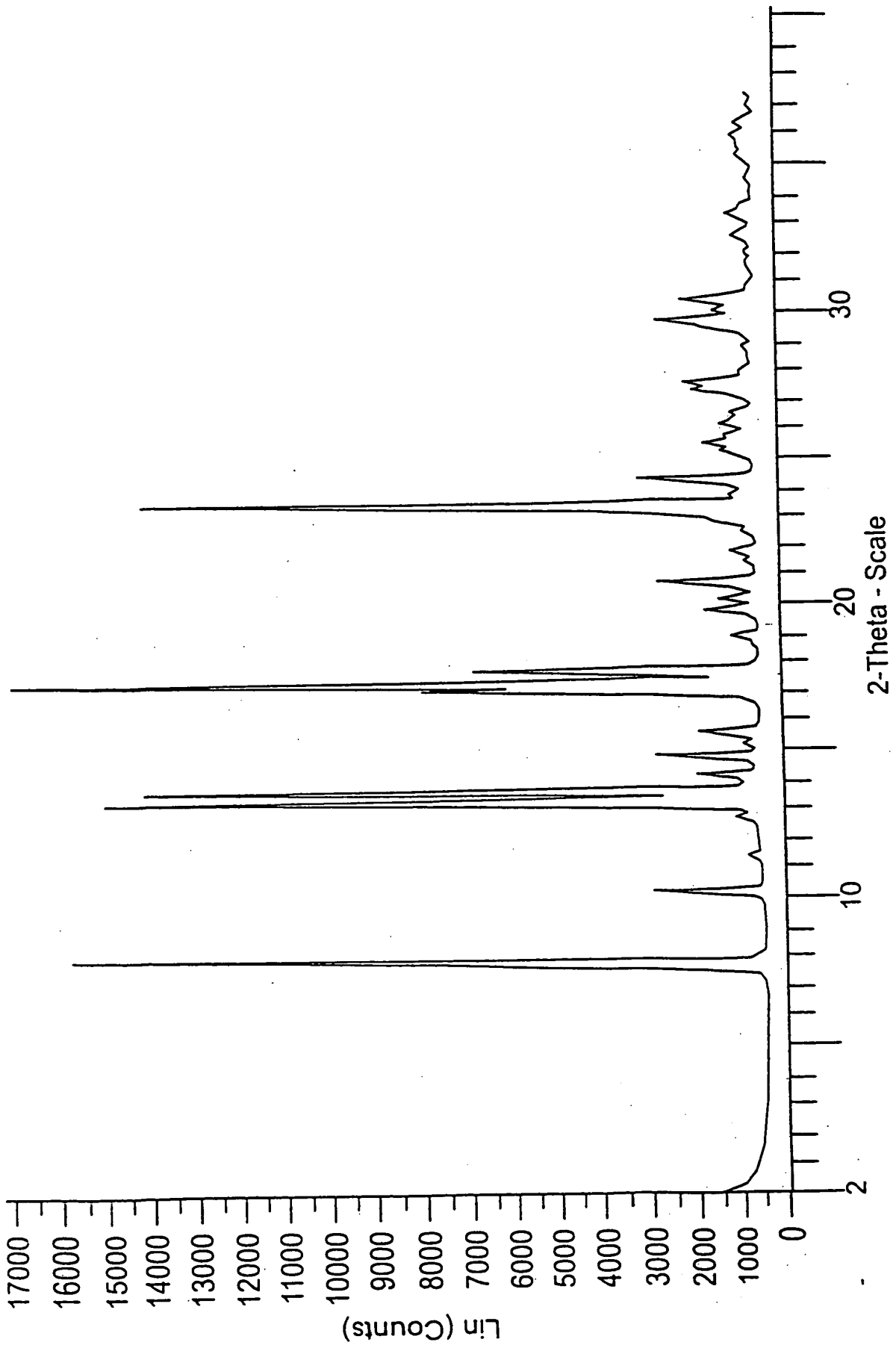

Lin (Counts)
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
2
10
20
30
2-Theta - Scale

FIGURE 2A

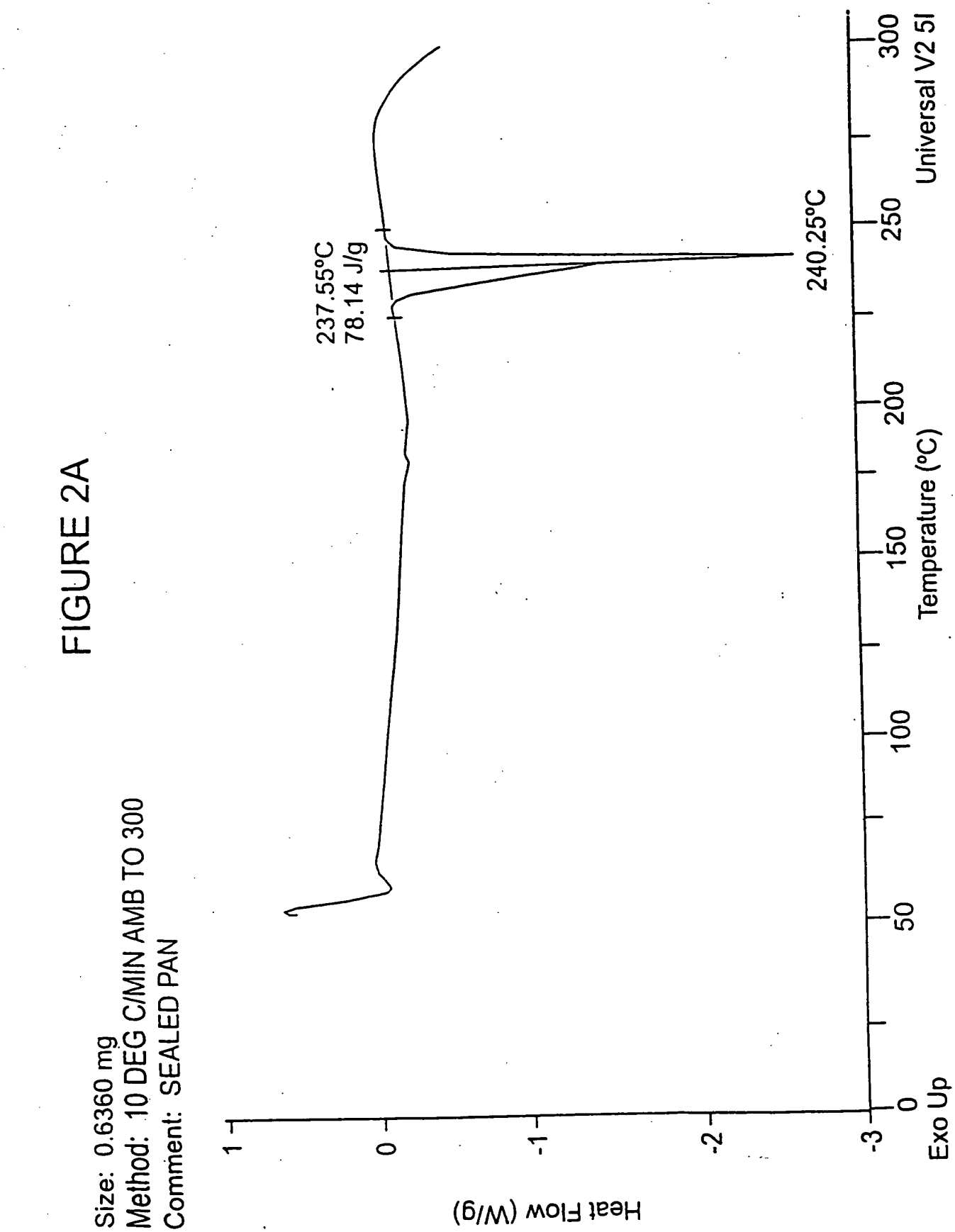

Size: 0.6360 mg
Method: 10 DEG C/MIN AMB TO 300
Comment: SEALED PAN
237.55°C
78.14 J/g
240.25°C
Heat Flow (W/g)
Exo Up
Temperature (°C)
Universal V2 5I
1
0
-1
-2
-3
0
50
100
150
200
250
300

FIGURE 2B

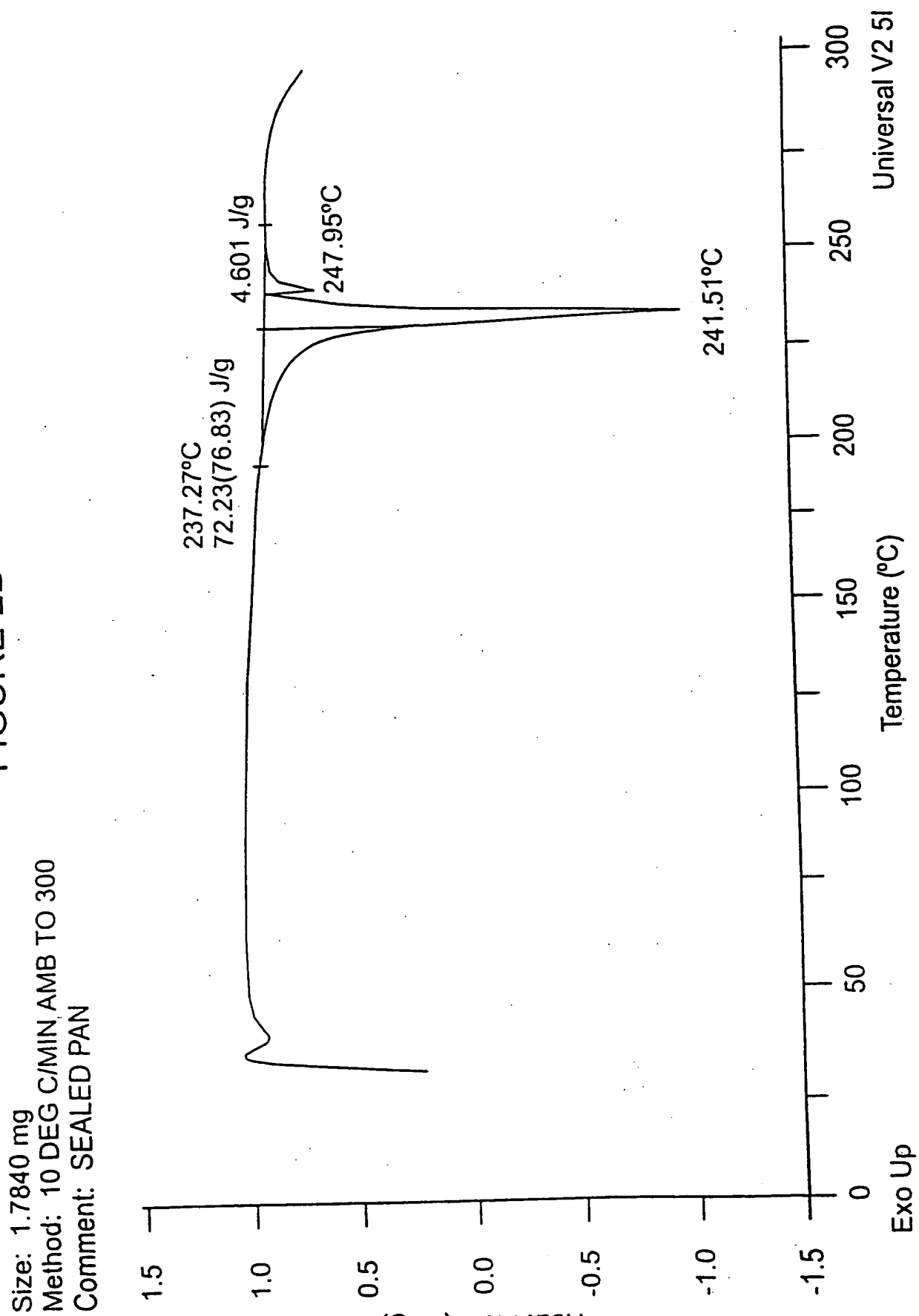

Size: 1.7840 mg
Method: 10 DEG C/MIN AMB TO 300
Comment: SEALED PAN
237.27°C
72.23(76.83) J/g
4.601 J/g
247.95°C
241.51°C
Heat Flow (W/g)
Exo Up
Temperature (°C)
Universal V2 5I
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
0
50
100
150
200
250
300

FIGURE 2C

Size: 1.4230 mg
Method: 10 DEG C/MIN AMB TO 300
Comment: SEALED PAN

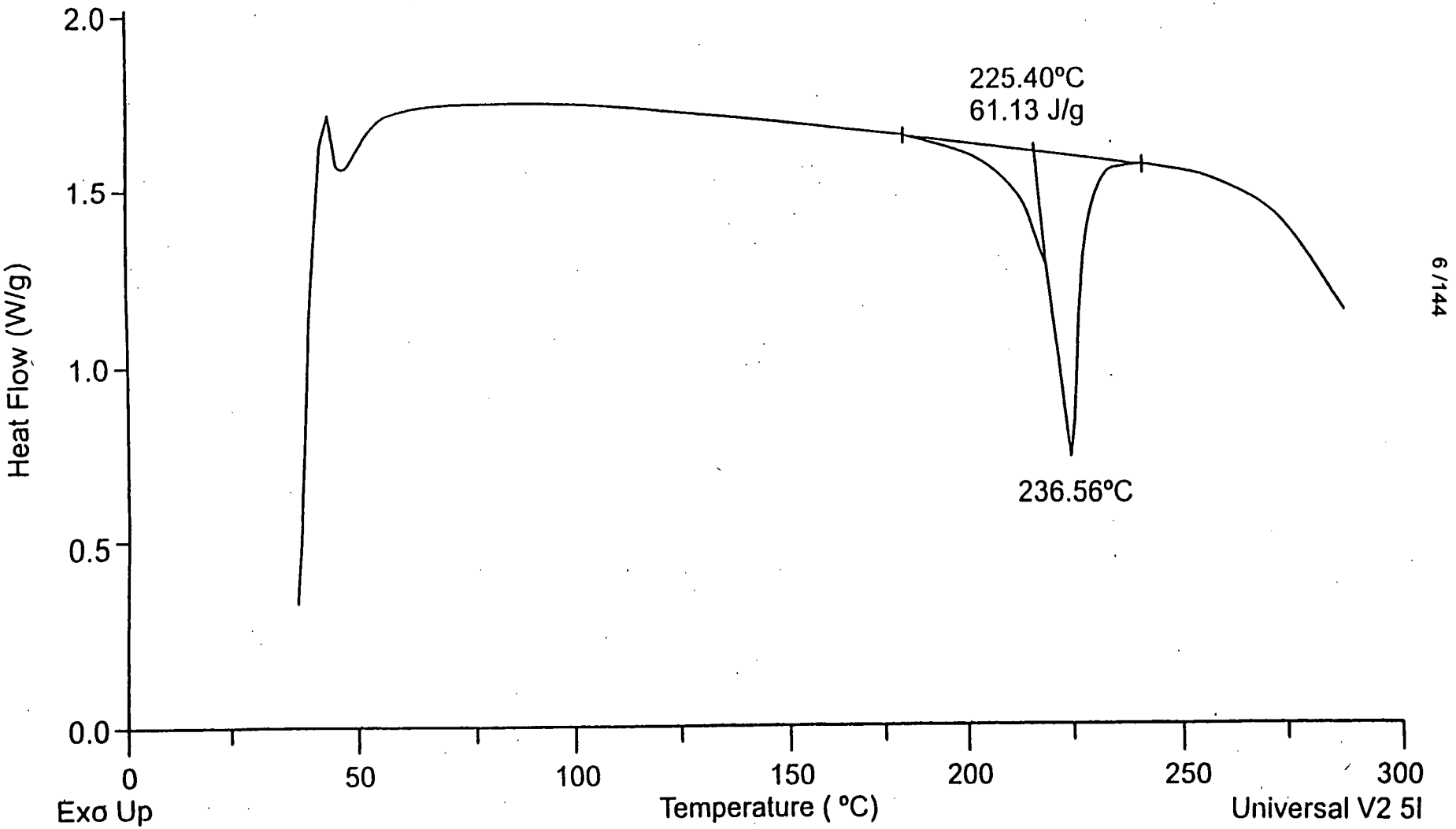


FIGURE 2D

Size: 1.0400 mg
Method: 10 DEG C/MIN AMB TO 300
Comment: SEALED PAN

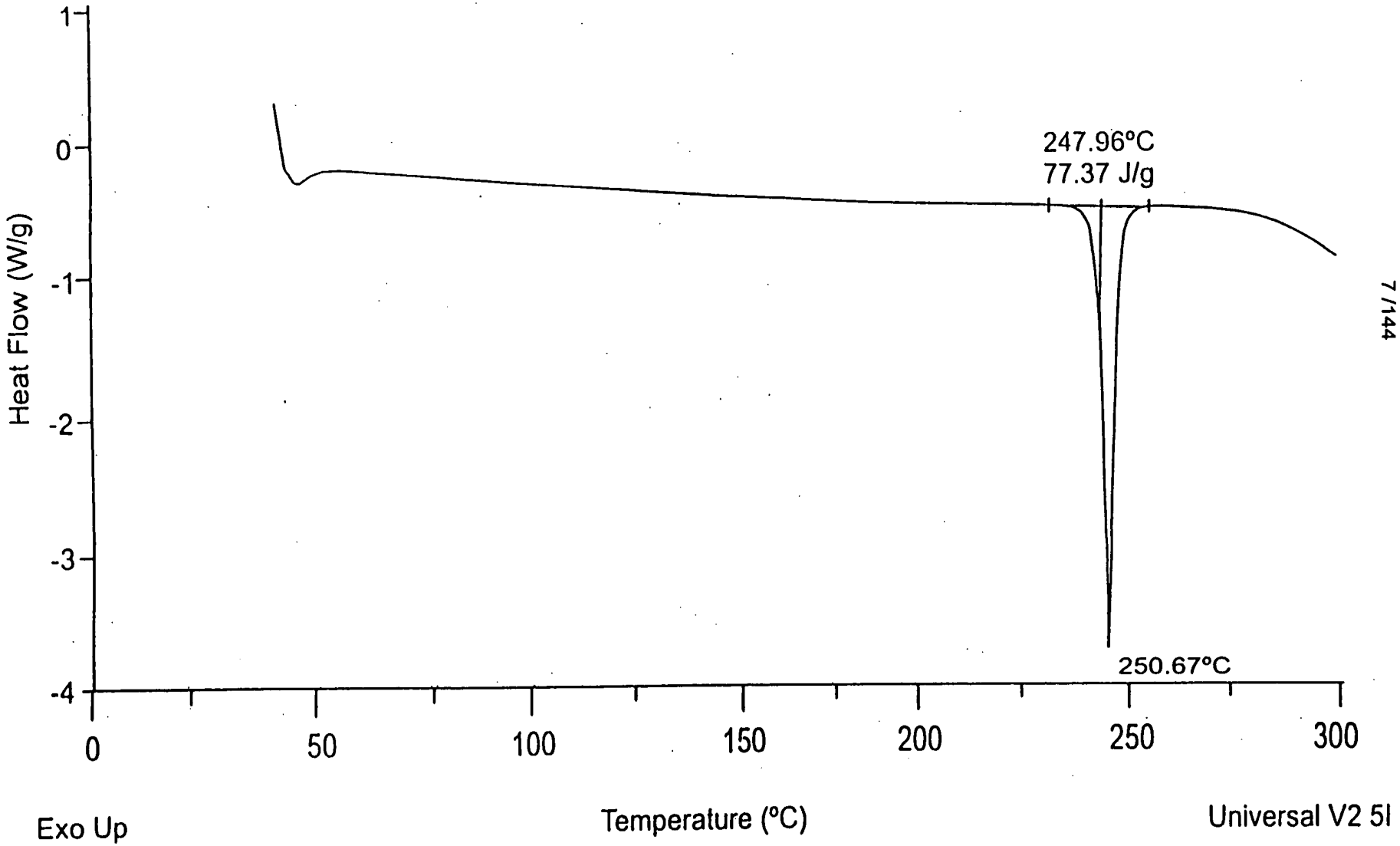


FIGURE 3A

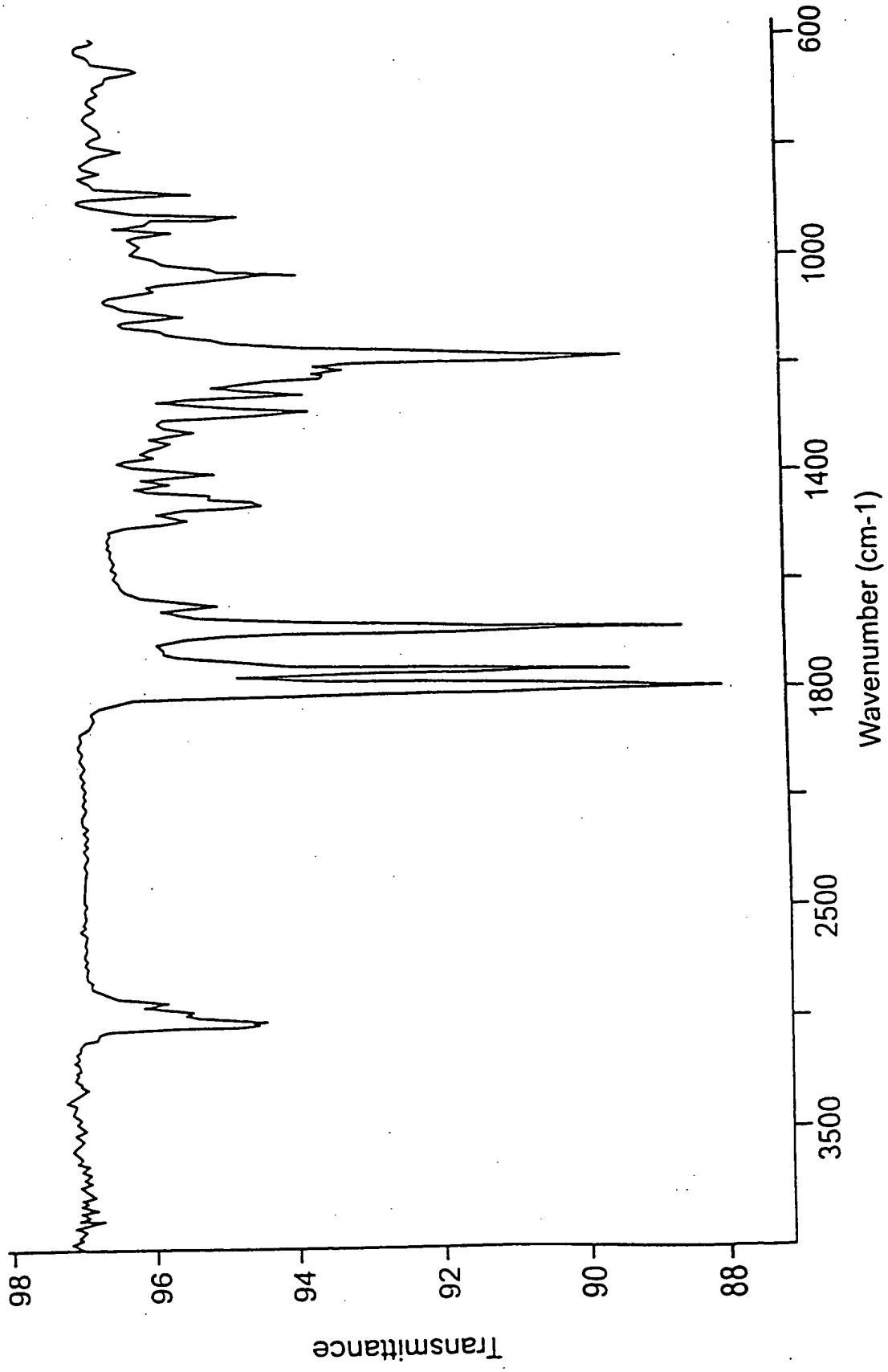

Transmittance
98
96
94
92
90
88
3500
2500
1800
1400
1000
600
Wavenumber (cm-1)

FIGURE 3B

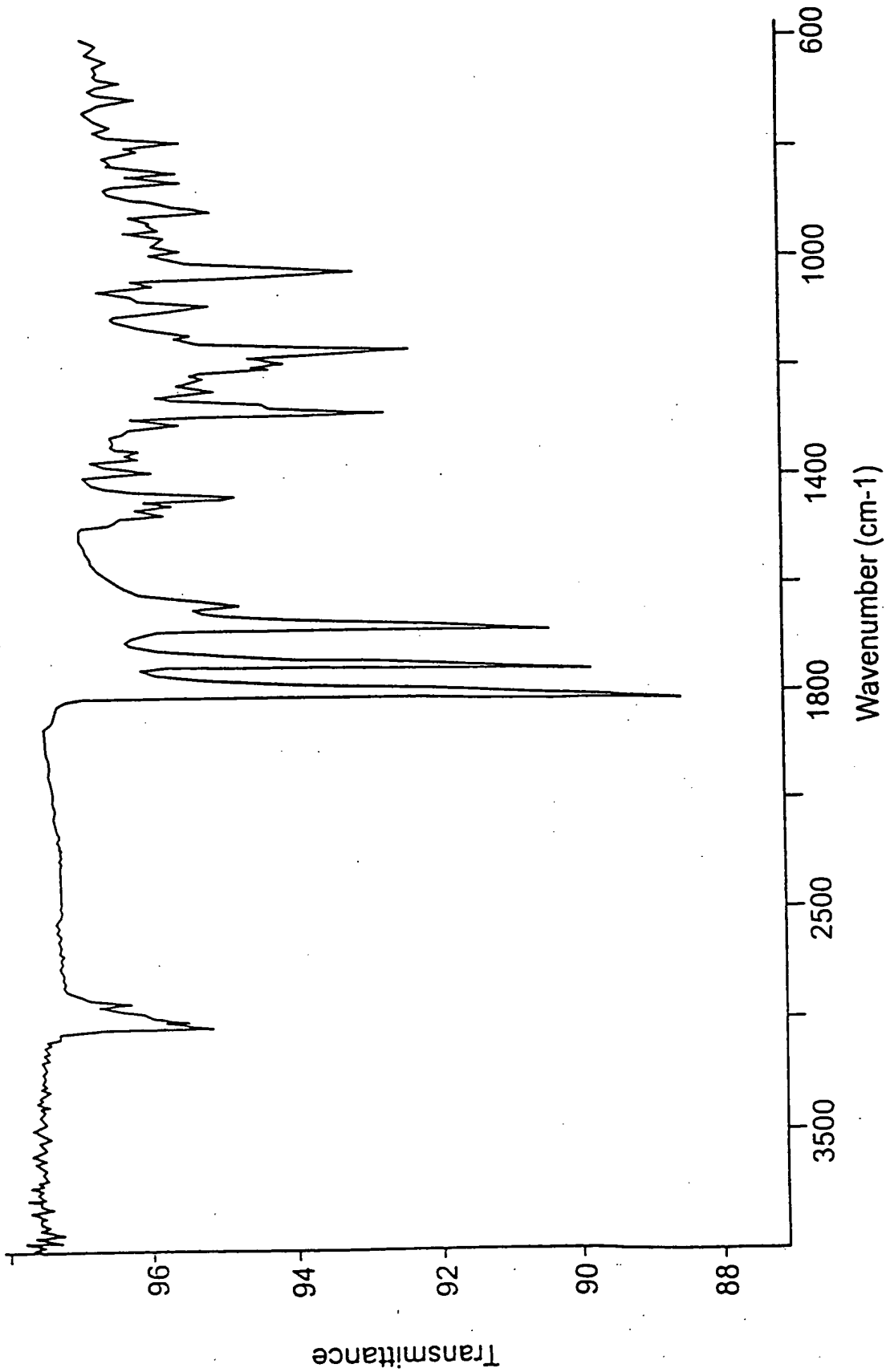

Transmittance
96
94
92
90
88
3500
2500
1800
1400
1000
600
Wavenumber (cm-1)

FIGURE 3C

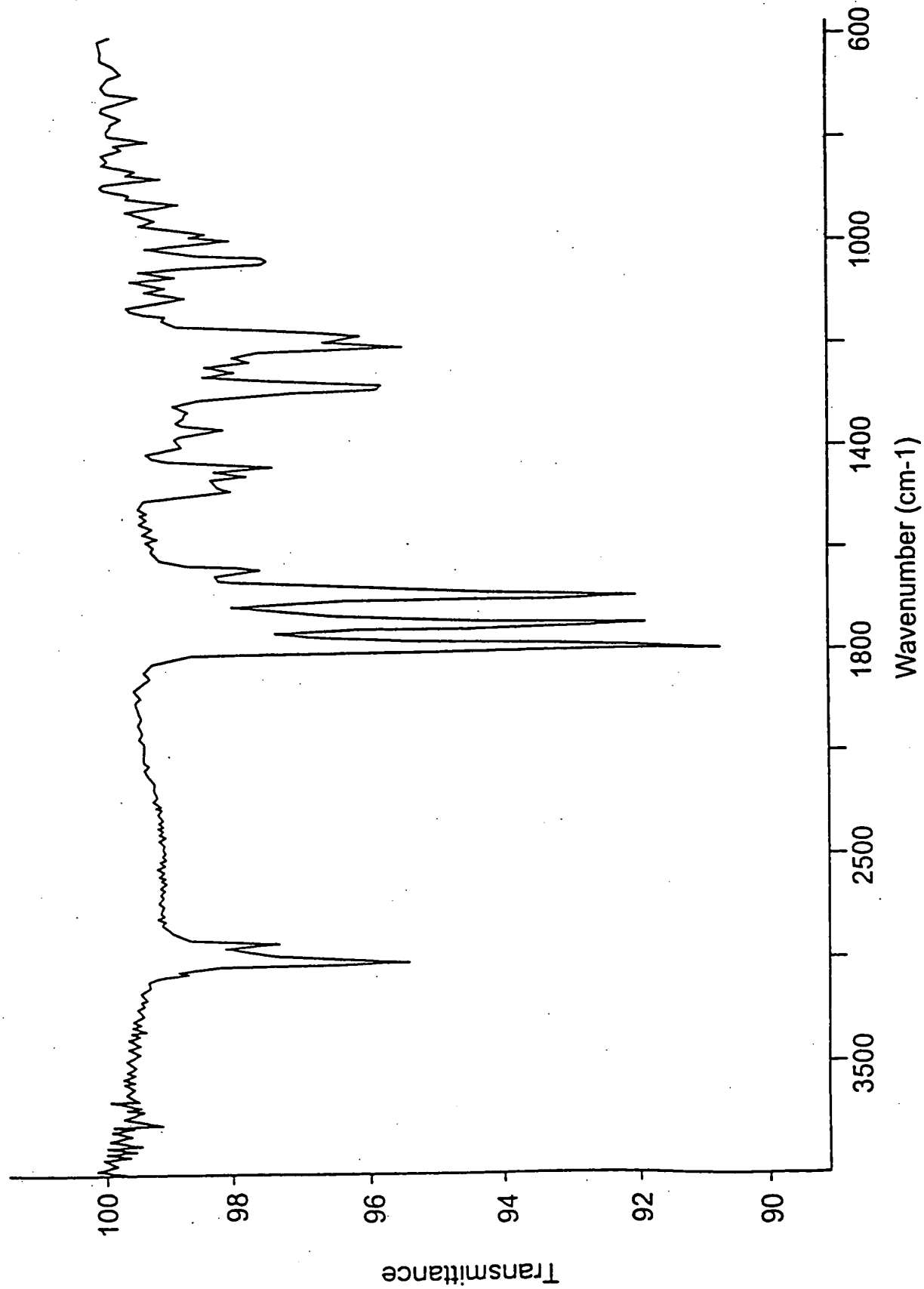

Transmittance
100
98
96
94
92
90
3500
2500
1800
1400
1000
600
Wavenumber (cm-1)

FIGURE 3D

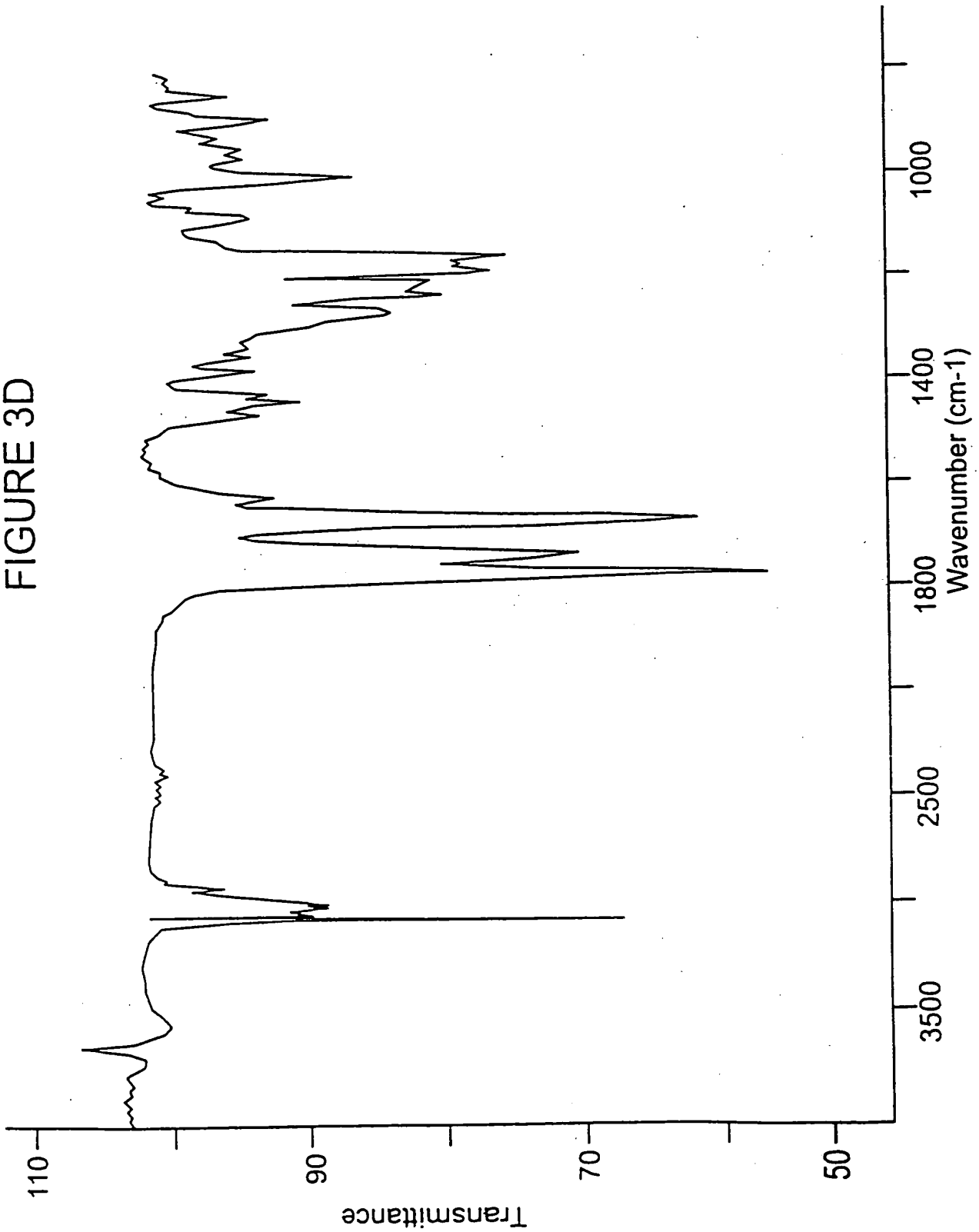
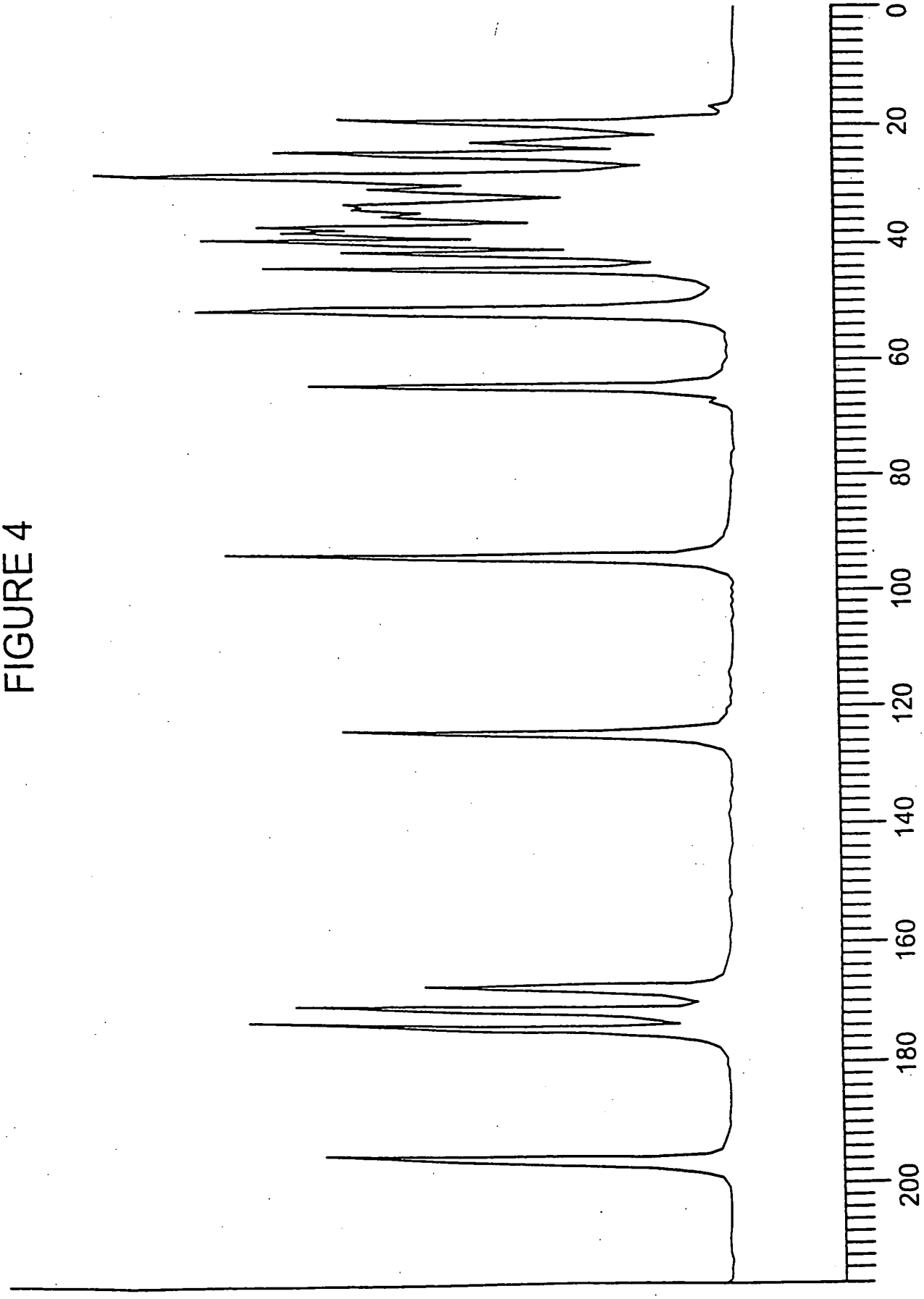

Transmittance
110
90
70
50
3500
2500
1800
1400
1000
Wavenumber (cm-1)

FIGURE 4



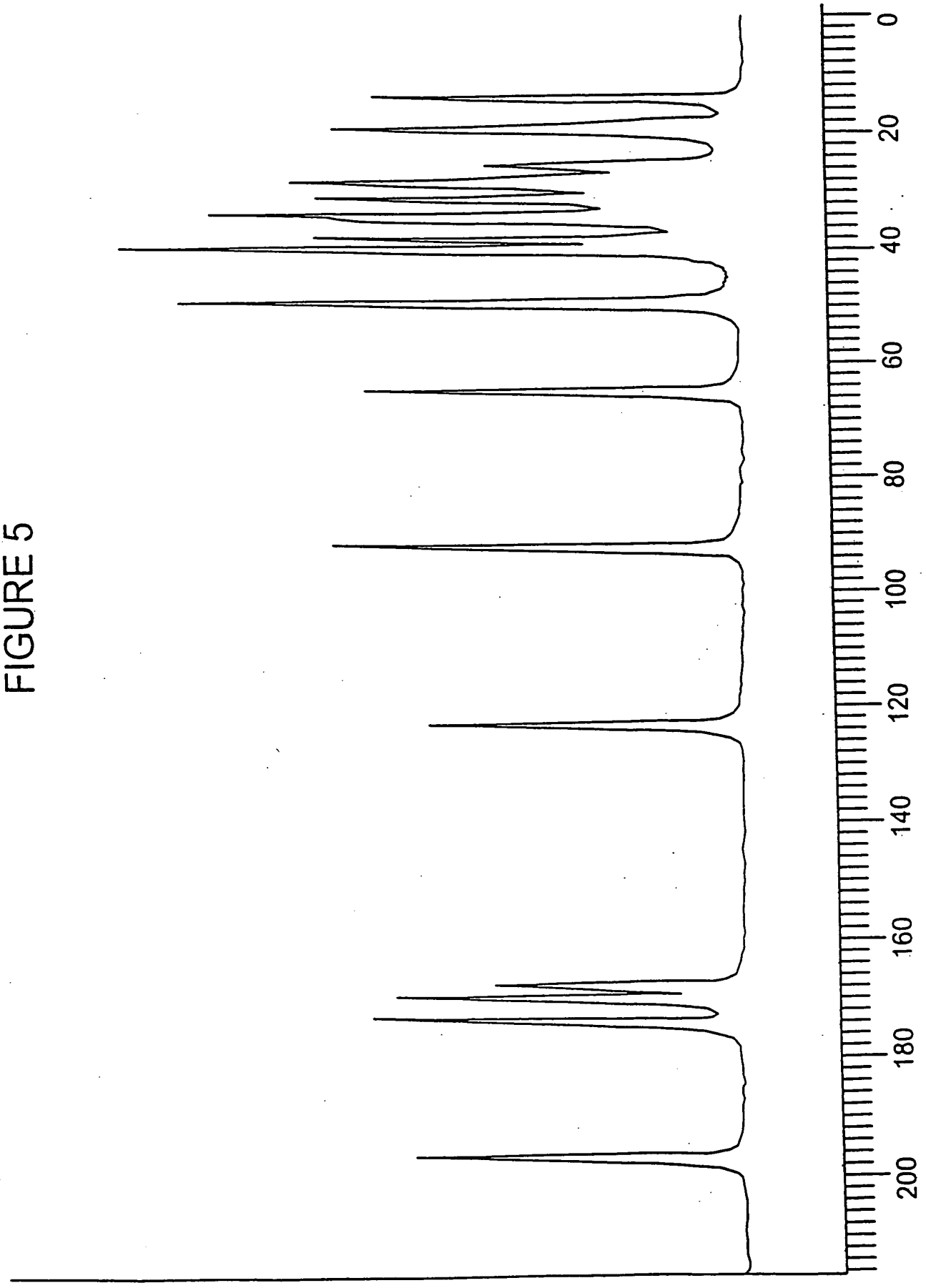


FIGURE 5

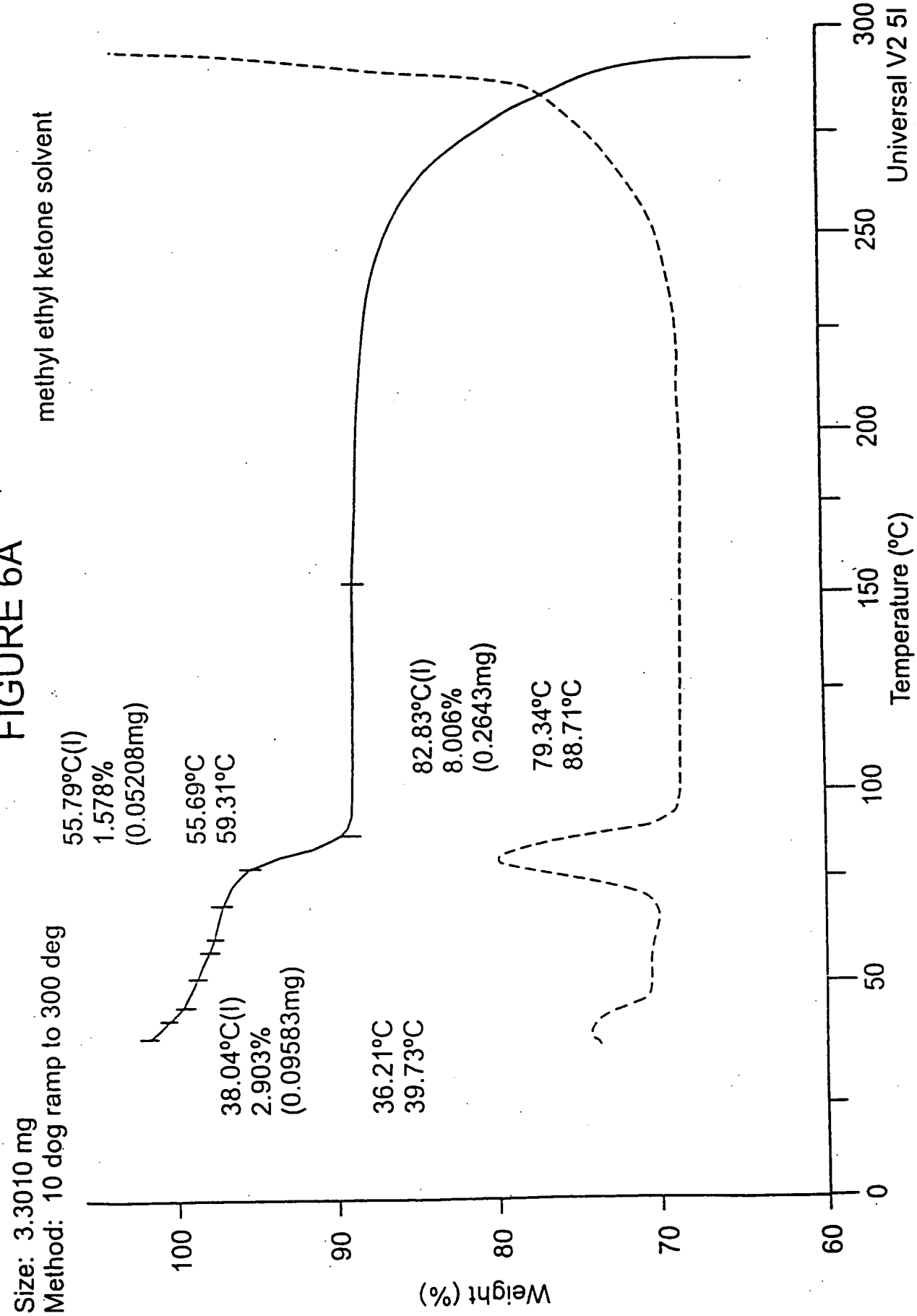


FIGURE 6A
methyl ethyl ketone solvent
Size: 3.3010 mg
Method: 10 dog ramp to 300 deg
55.79°C(l)
1.578%
(0.05208mg)
55.69°C
59.31°C
38.04°C(l)
2.903%
(0.09583mg)
36.21°C
39.73°C
82.83°C(l)
8.006%
(0.2643mg)
79.34°C
88.71°C
Weight (%)
100
90
80
70
60
0
50
100
150
200
250
300
Temperature (°C)
Universal V2 5I

FIGURE 7

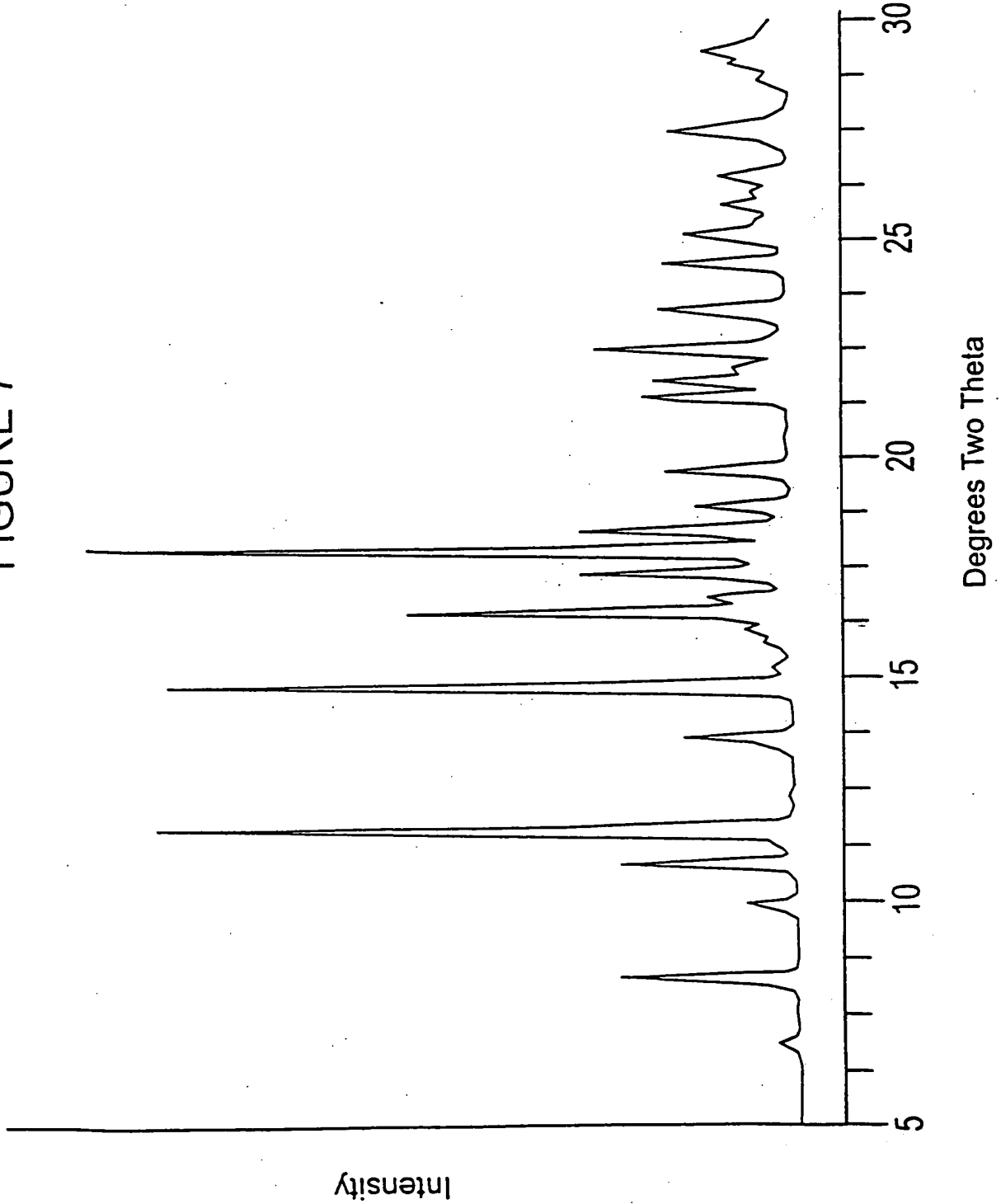


FIGURE 8

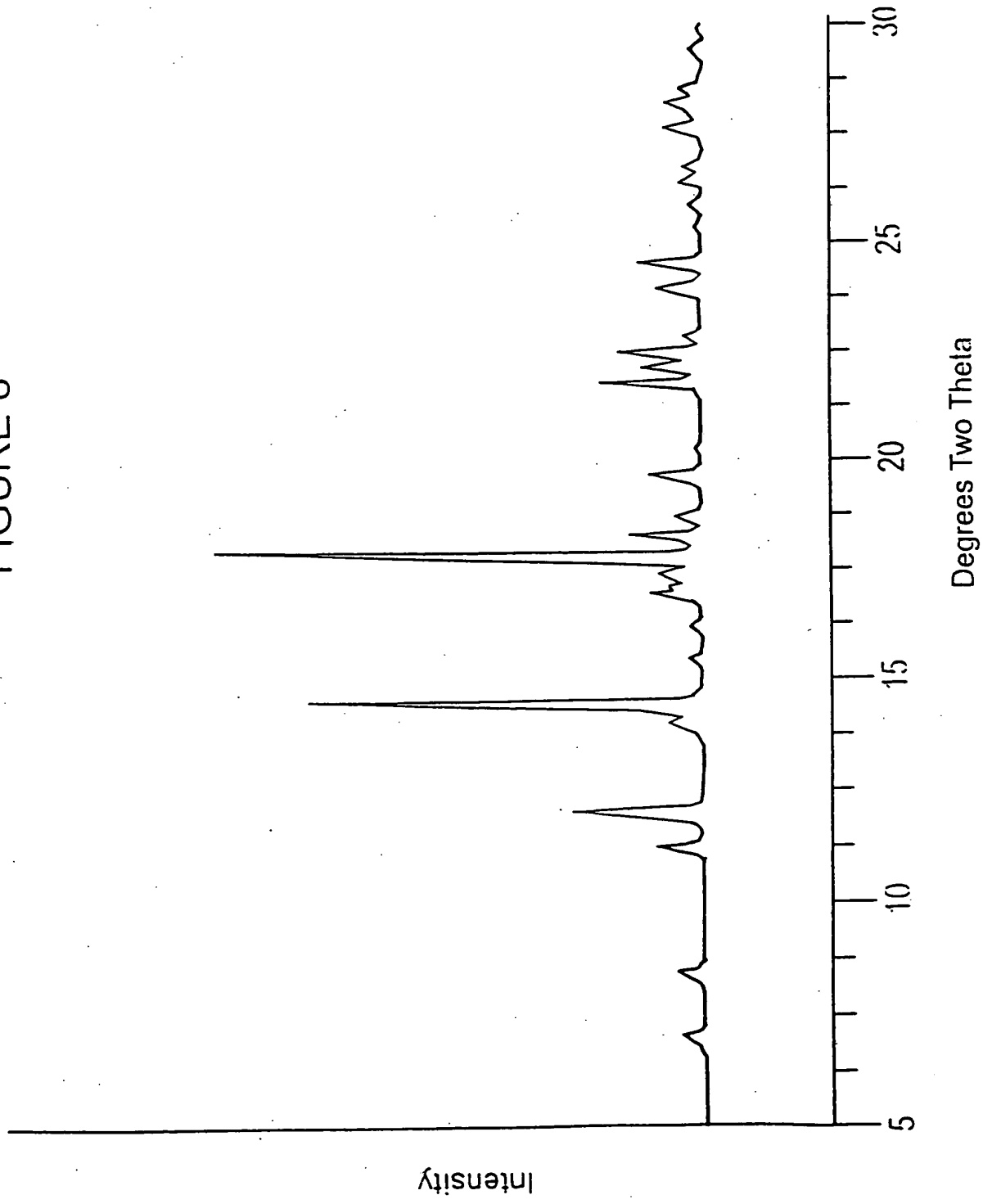
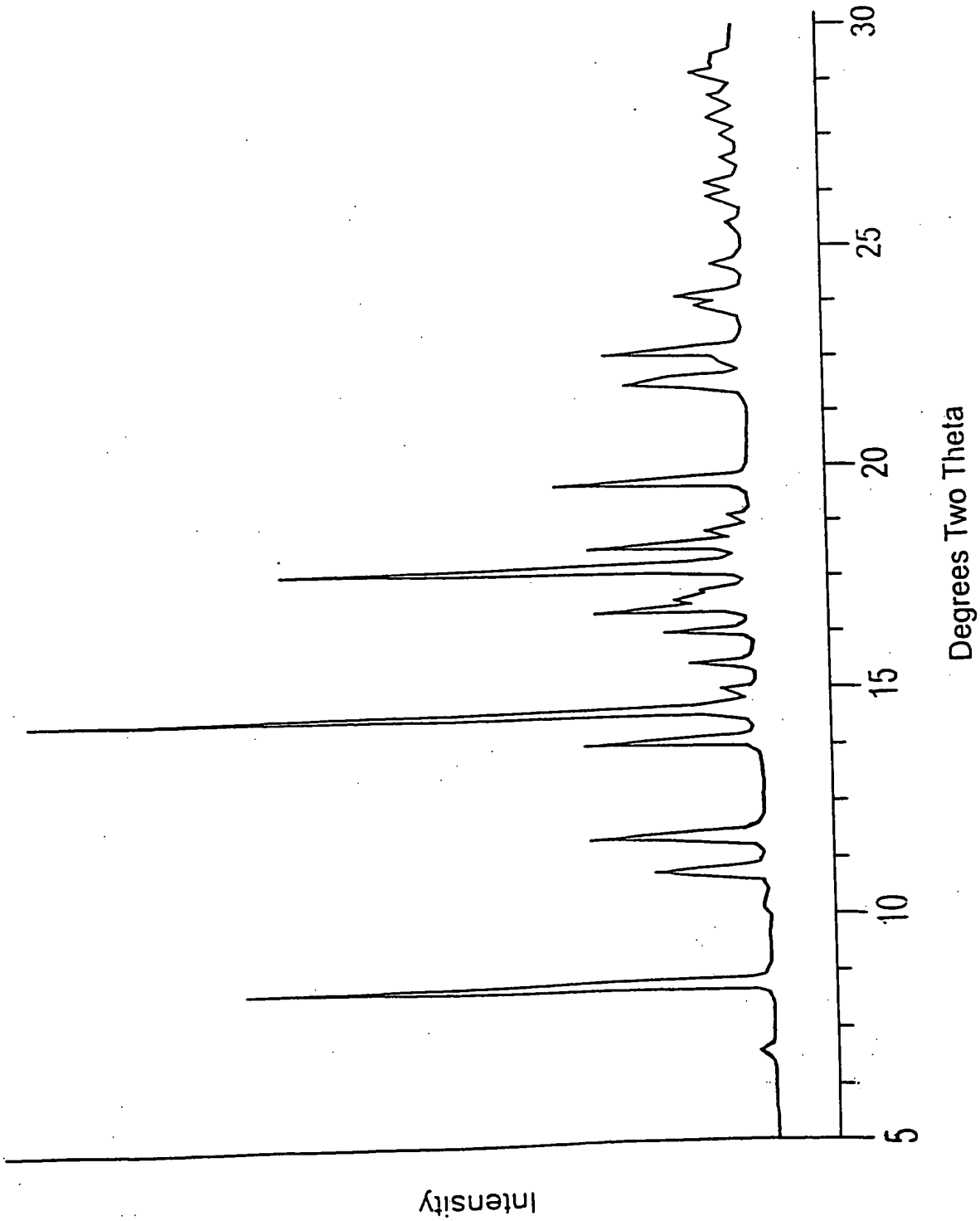


FIGURE 9



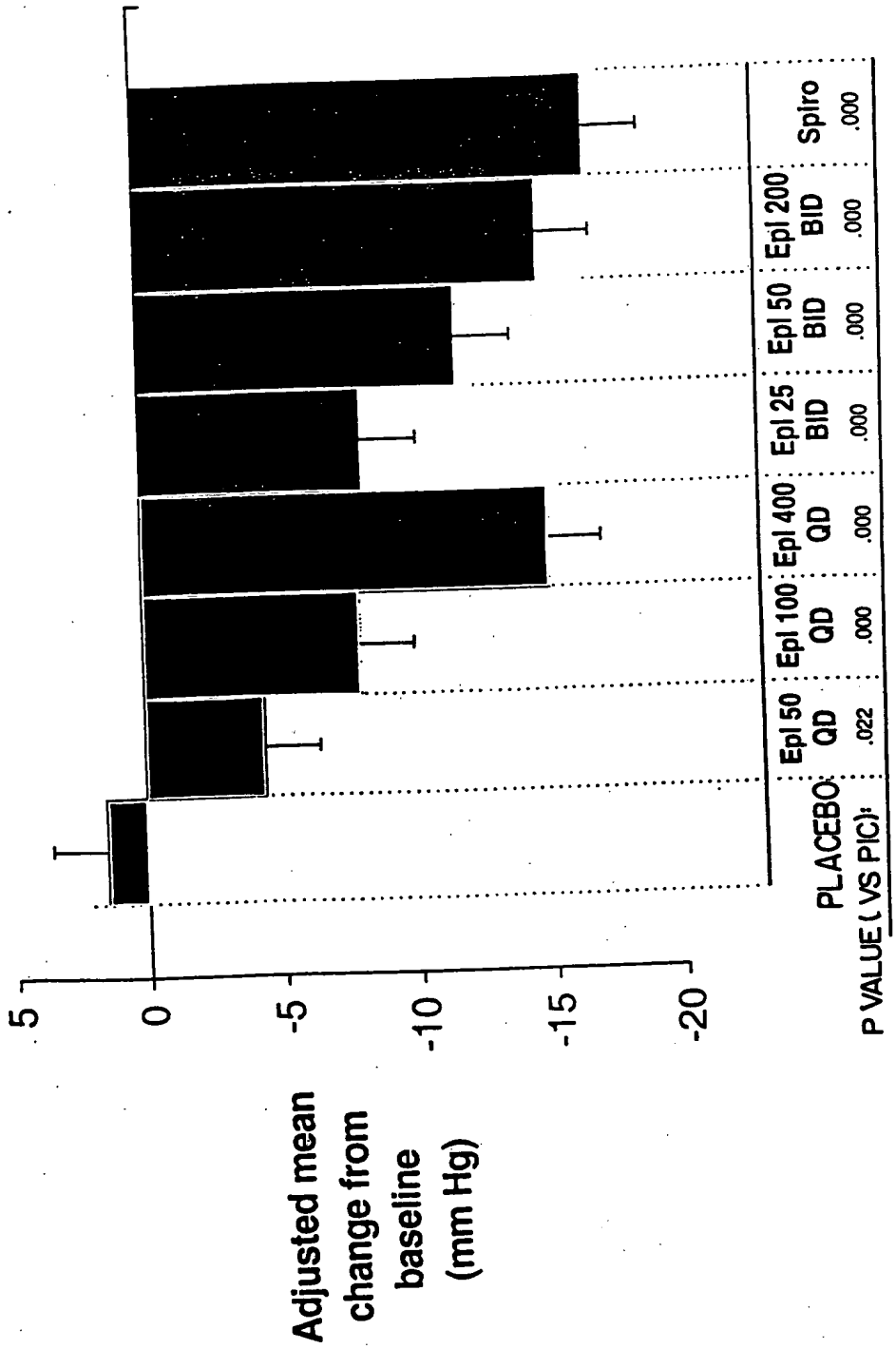

Adjusted mean change from baseline (mm Hg)
5
0
-5
-10
-15
-20
PLACEBO
Epl 50 QD
Epl 100 QD
Epl 400 QD
Epl 25 BID
Epl 50 BID
Epl 200 BID
Spiro
P VALUE (VS PIC)
.022
.000
.000
.000
.000
.000
.000

Figure 10

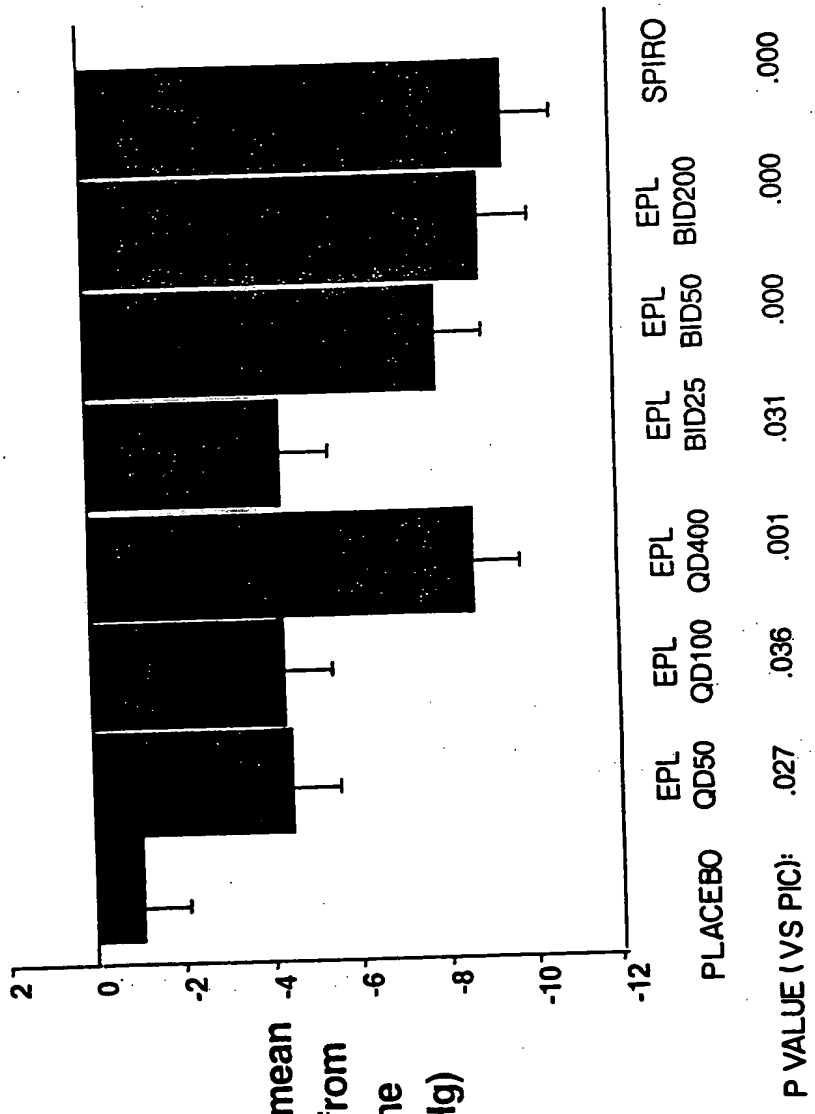

Adjusted mean change from baseline (mm Hg)
2
0
-2
-4
-6
-8
-10
-12
PLACEBO
EPL QD50
EPL QD100
EPL QD400
EPL BID25
EPL BID50
EPL BID200
SPIRO
P VALUE (VS PIC):
.027
.036
.001
.031
.000
.000
.000

Figure 11

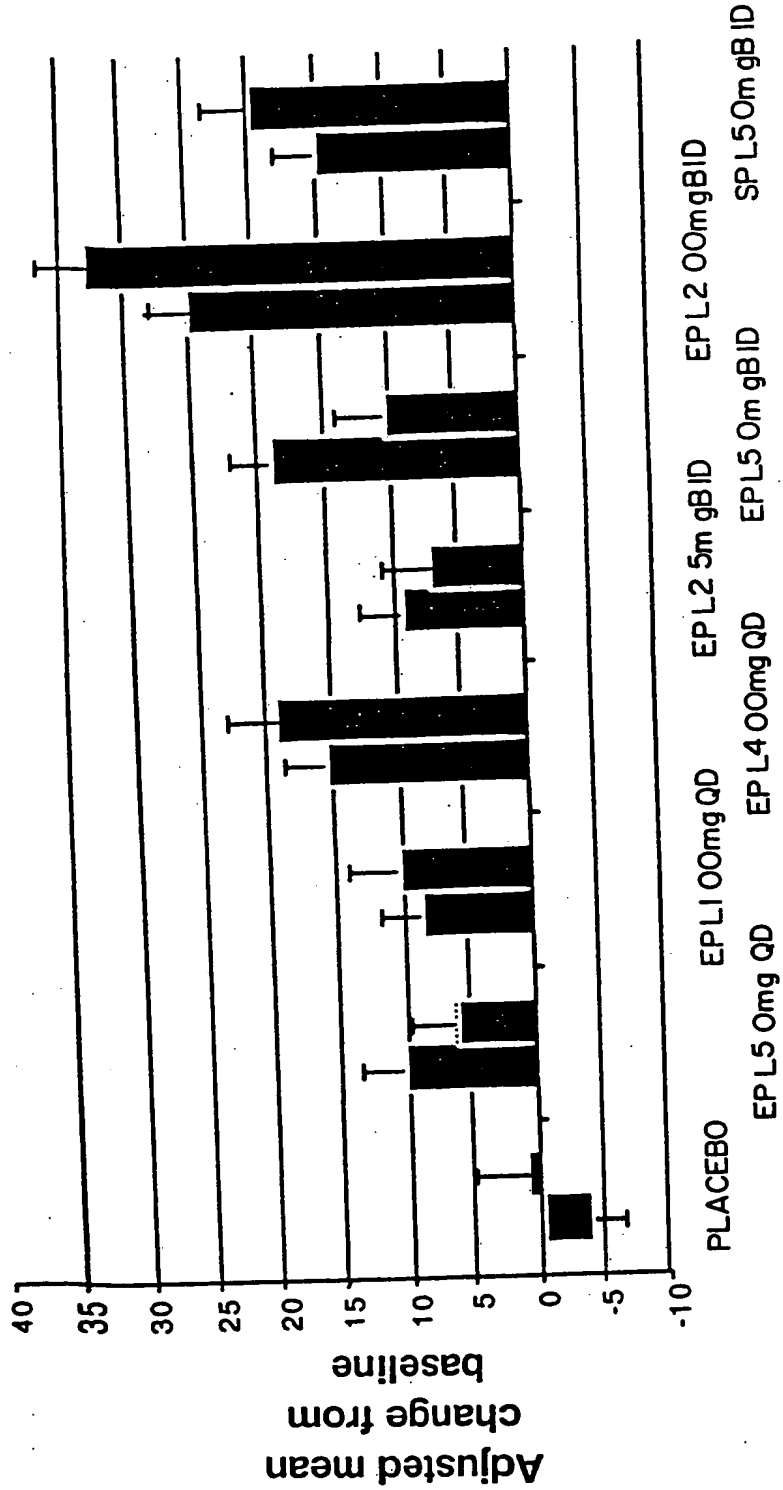

Adjusted mean change from baseline
40
35
30
25
20
15
10
5
0
-5
-10
PLACEBO
EP L5 0mg QD
EP L1 00mg QD
EP L4 00mg QD
EP L2 5m gB ID
EP L5 0m gB ID
EP L2 00mgBID
EP L5 0m gB ID
SP L5 0m gB ID
Renin-Active (MU/L)
Aldosterone (NG/L)

Figure 12

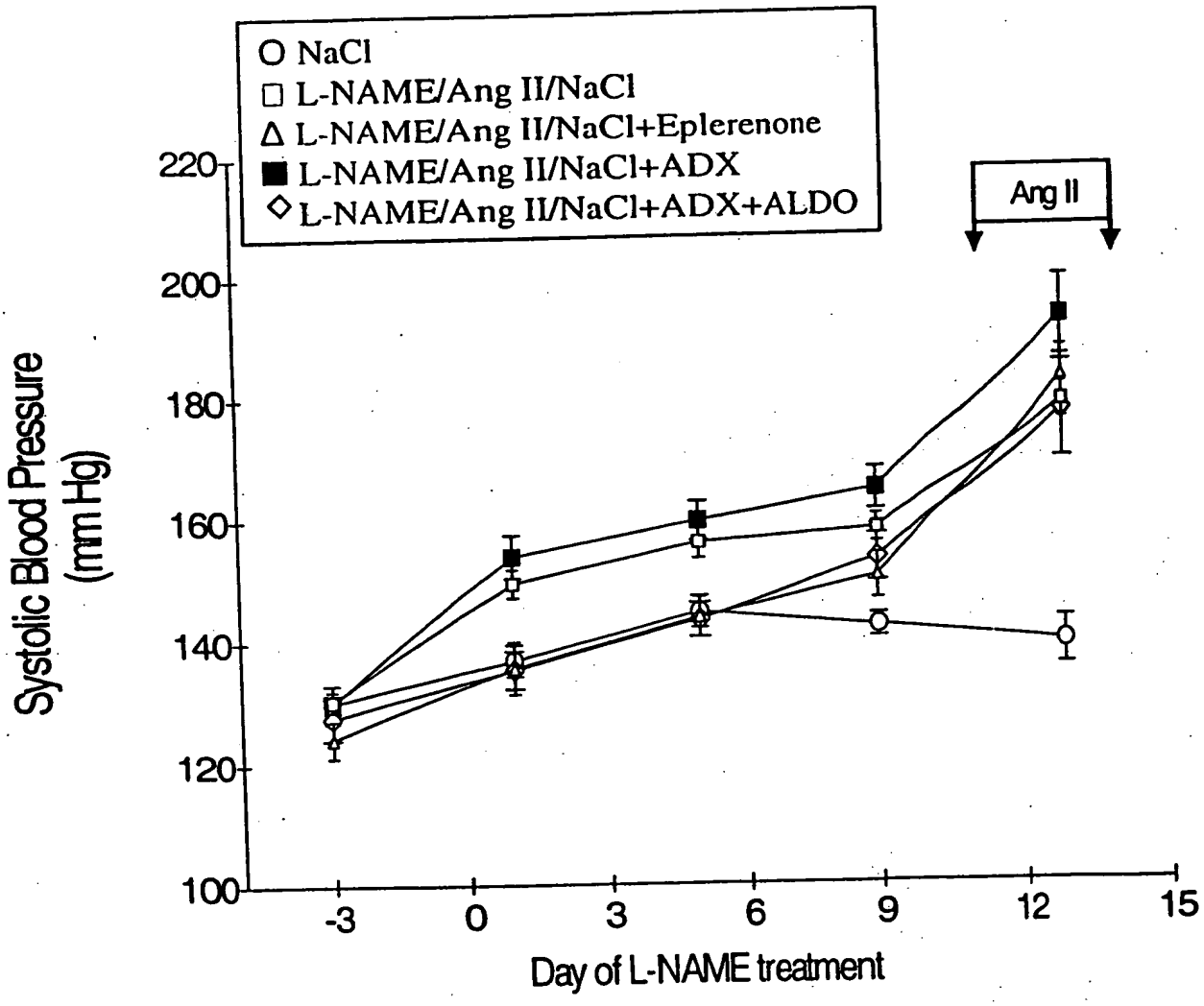


Figure A-1. Systolic blood pressure.

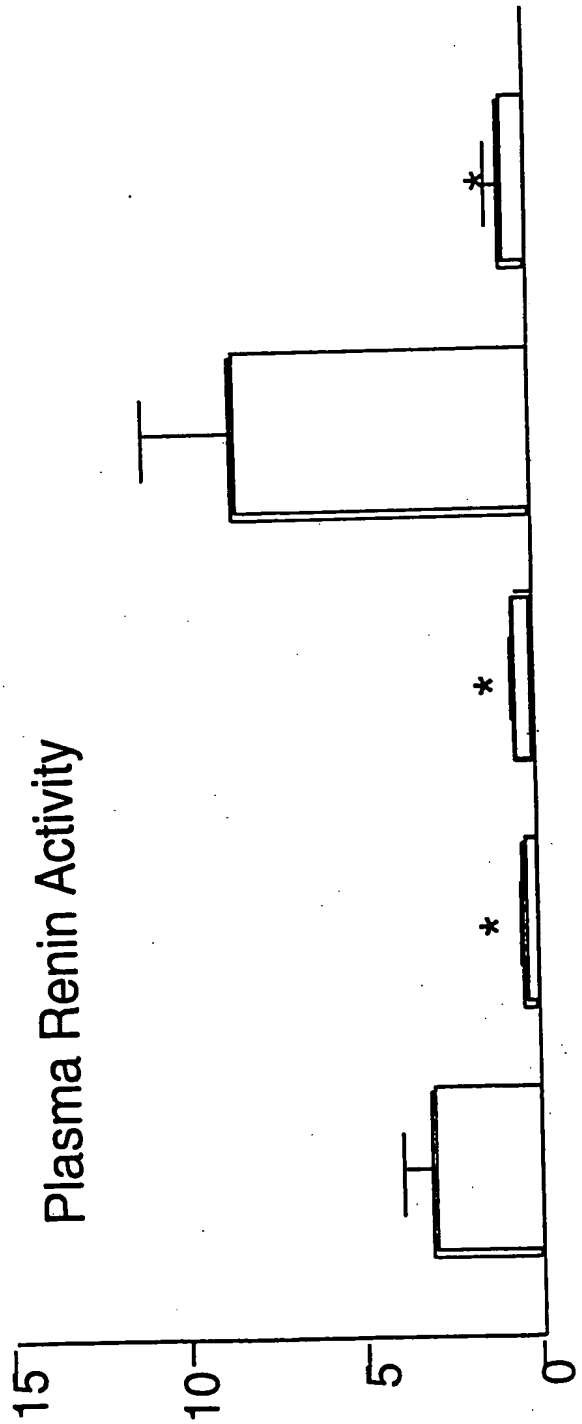


Figure A-2 (A) Plasma renin activity determined after sacrifice.

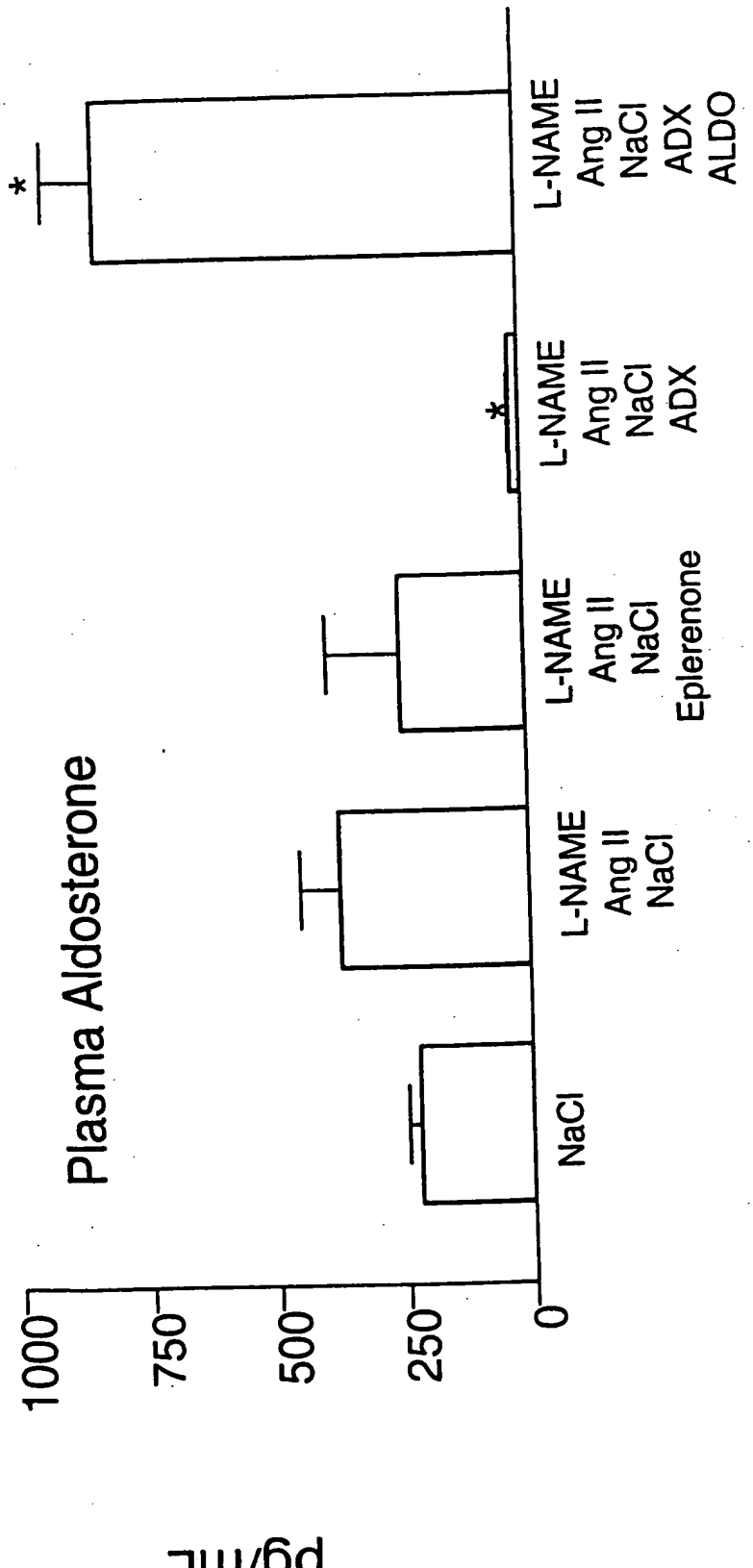
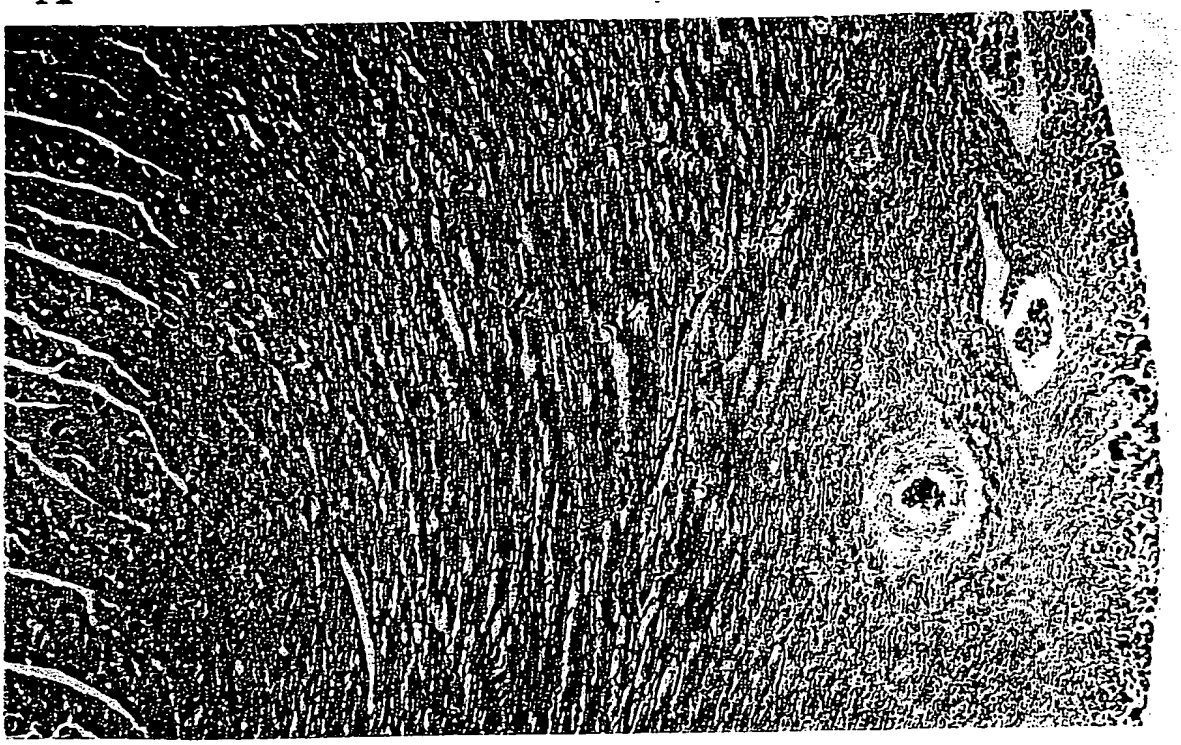


Figure A-2 (B) **Plasma aldosterone** levels determined after sacrifice.

FIGURE A-3

A



B

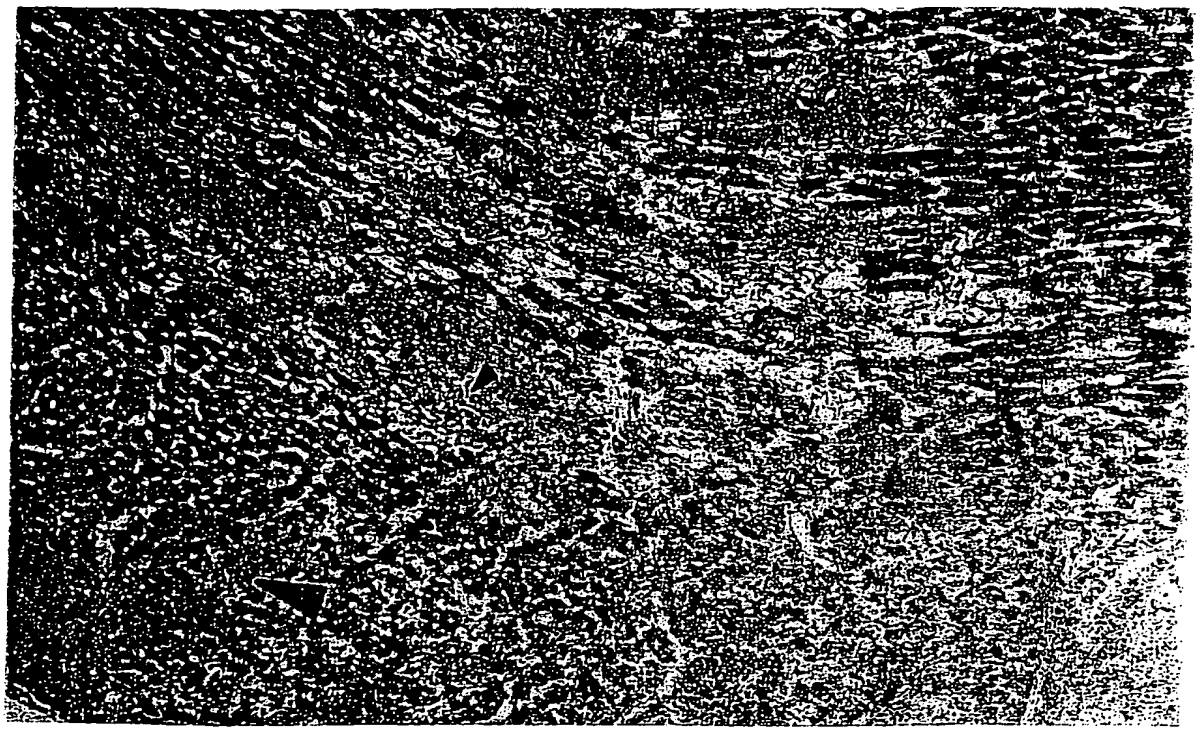
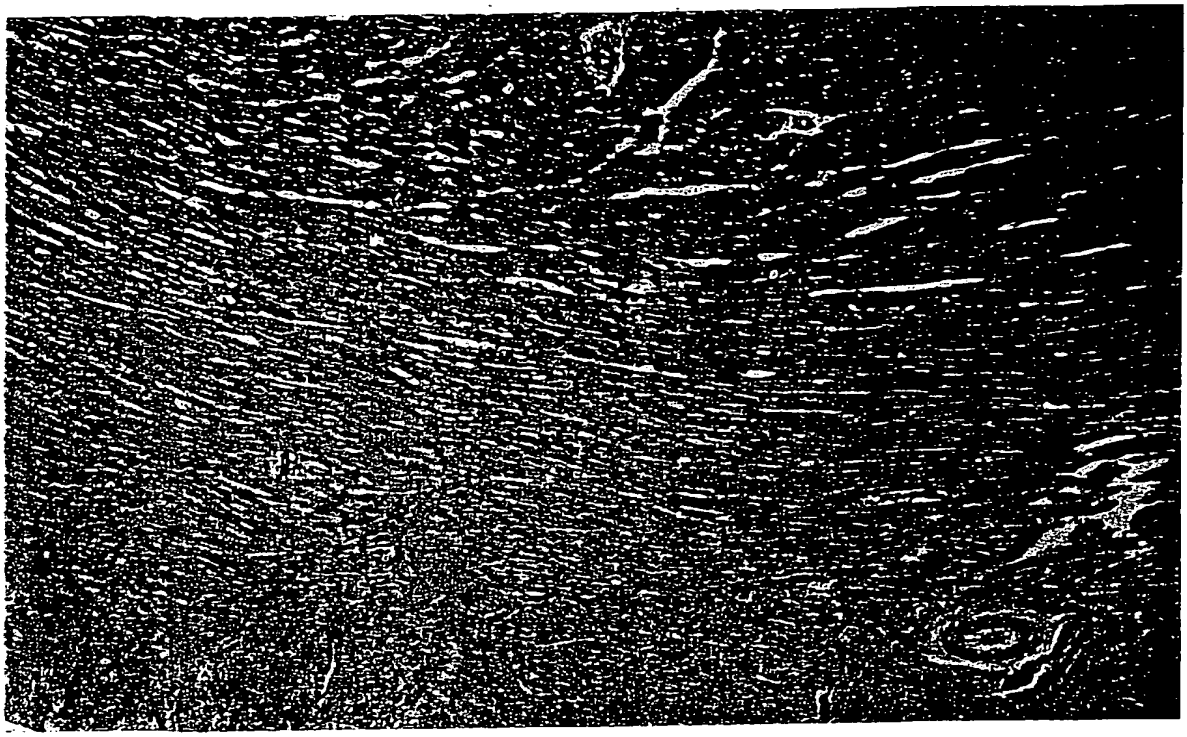
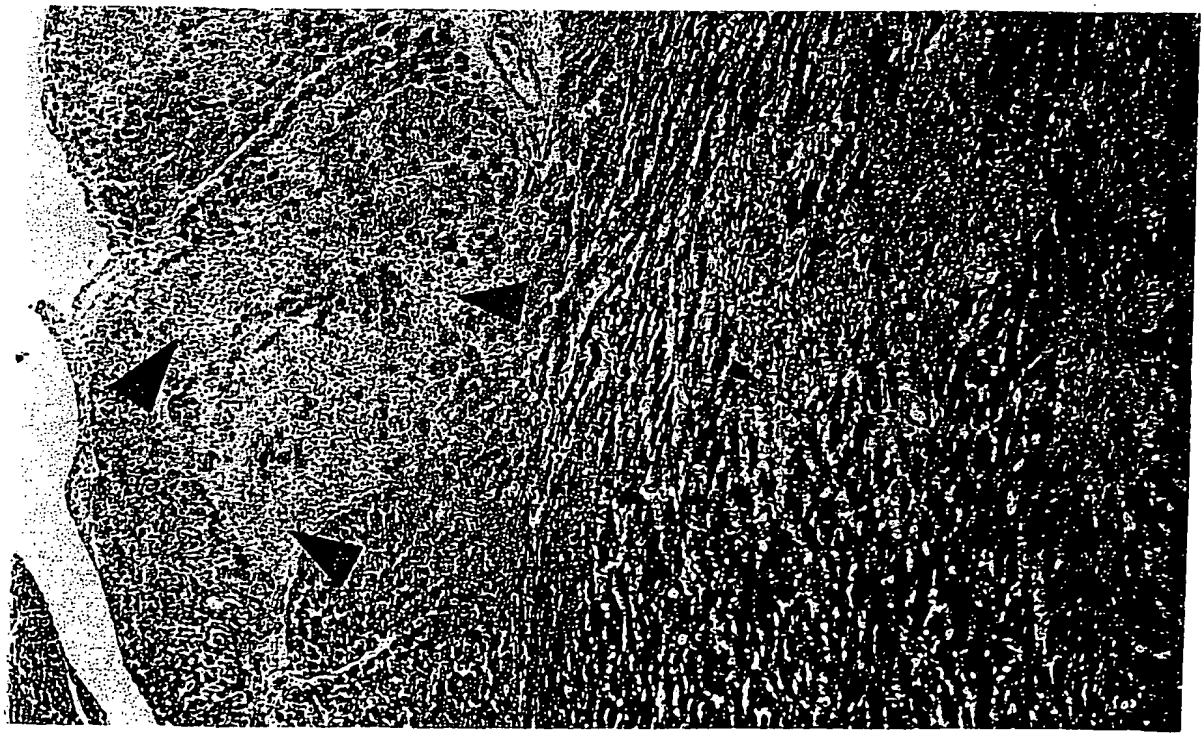


FIGURE A-3

C



D



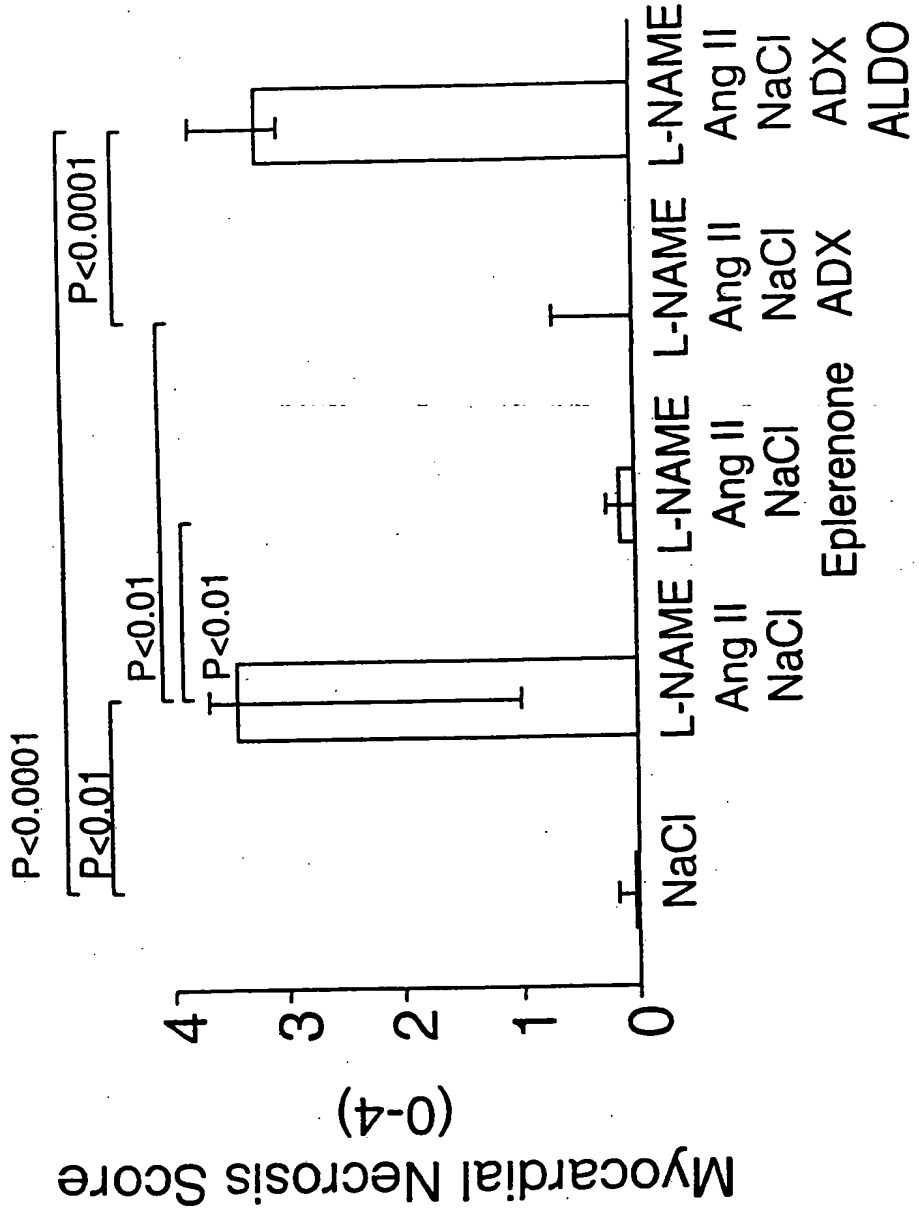


Figure A-4. Histopathologic scores for myocardial necrosis.

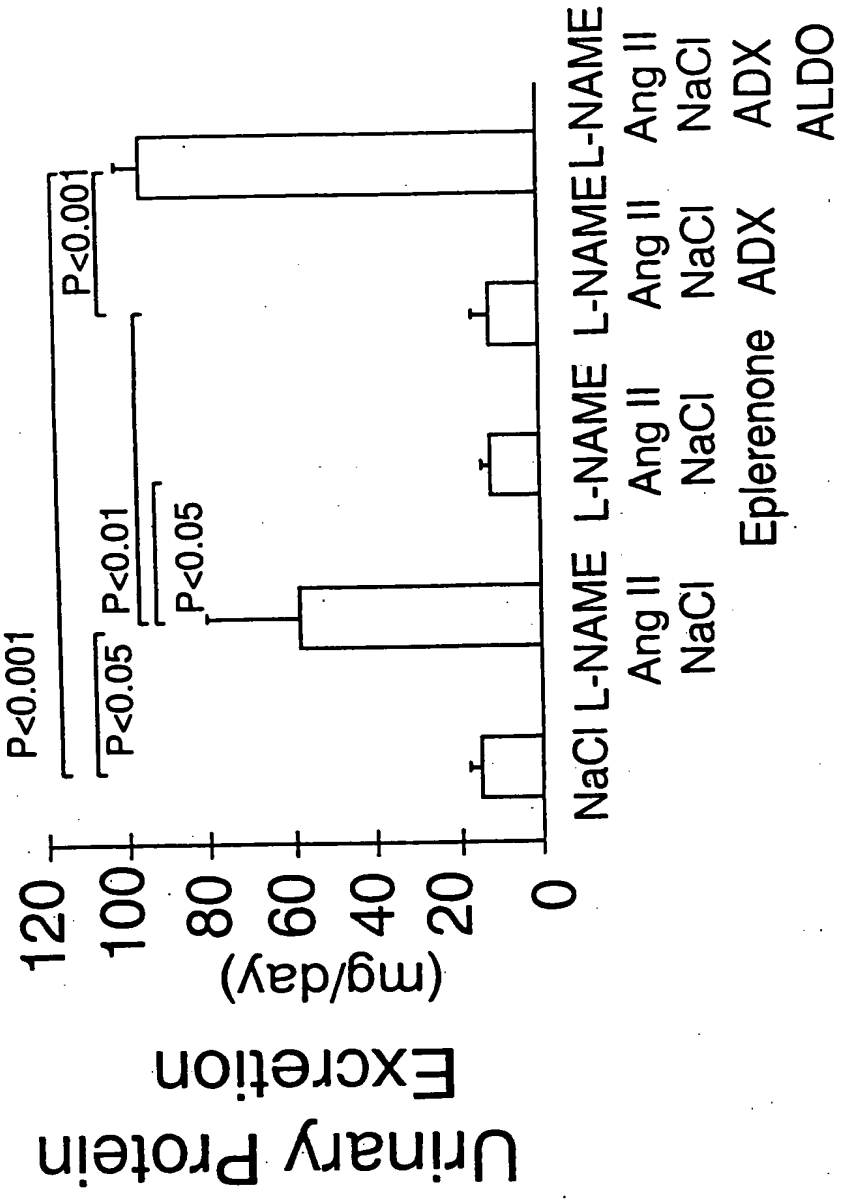
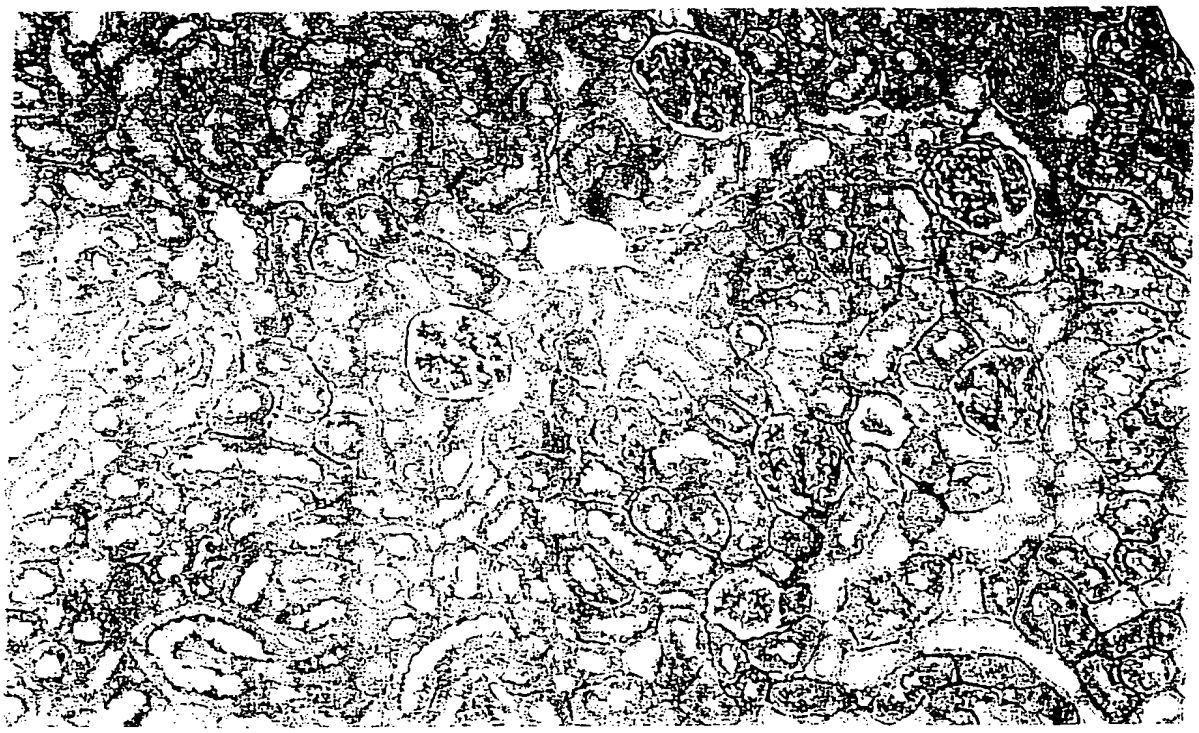


Figure A-5. Urinary protein excretion.

FIGURE A-6

A



B

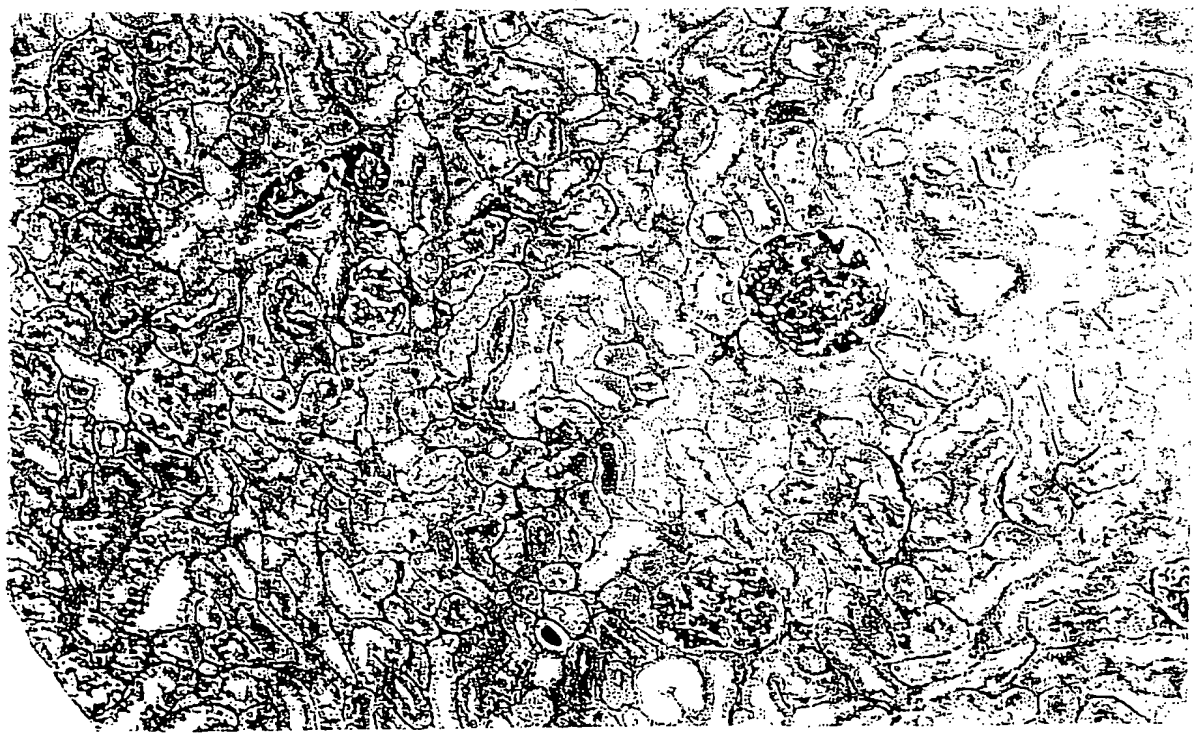
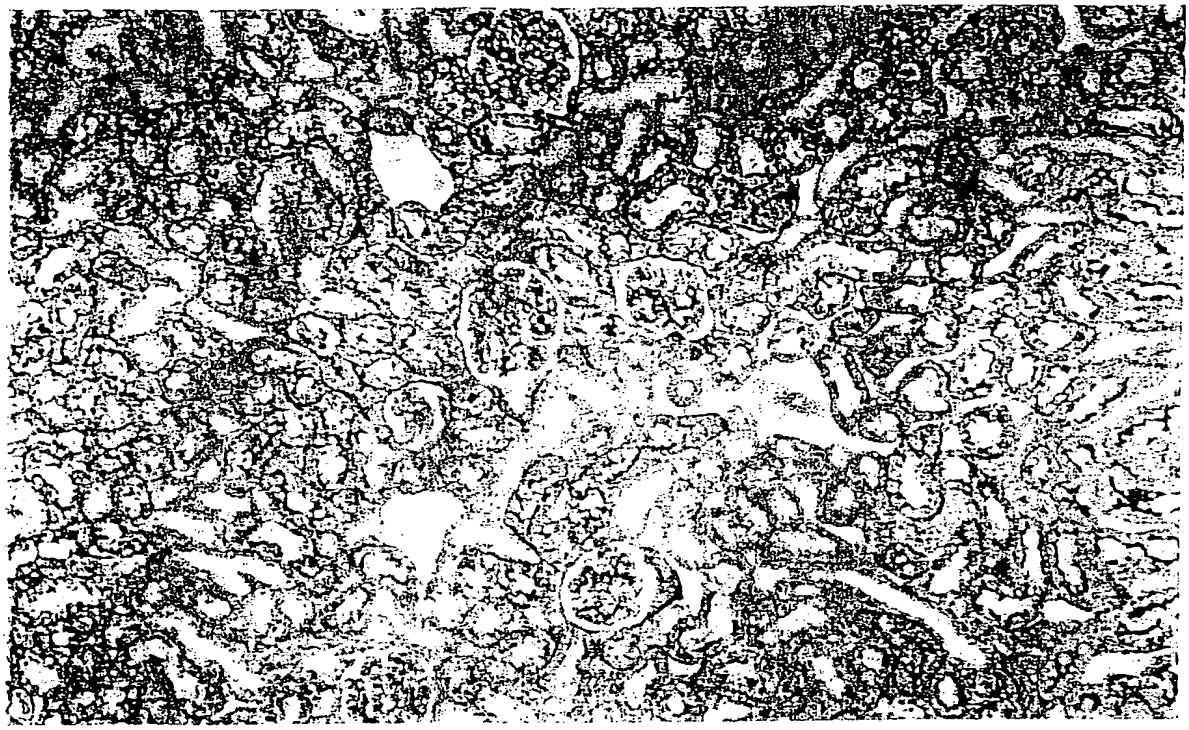
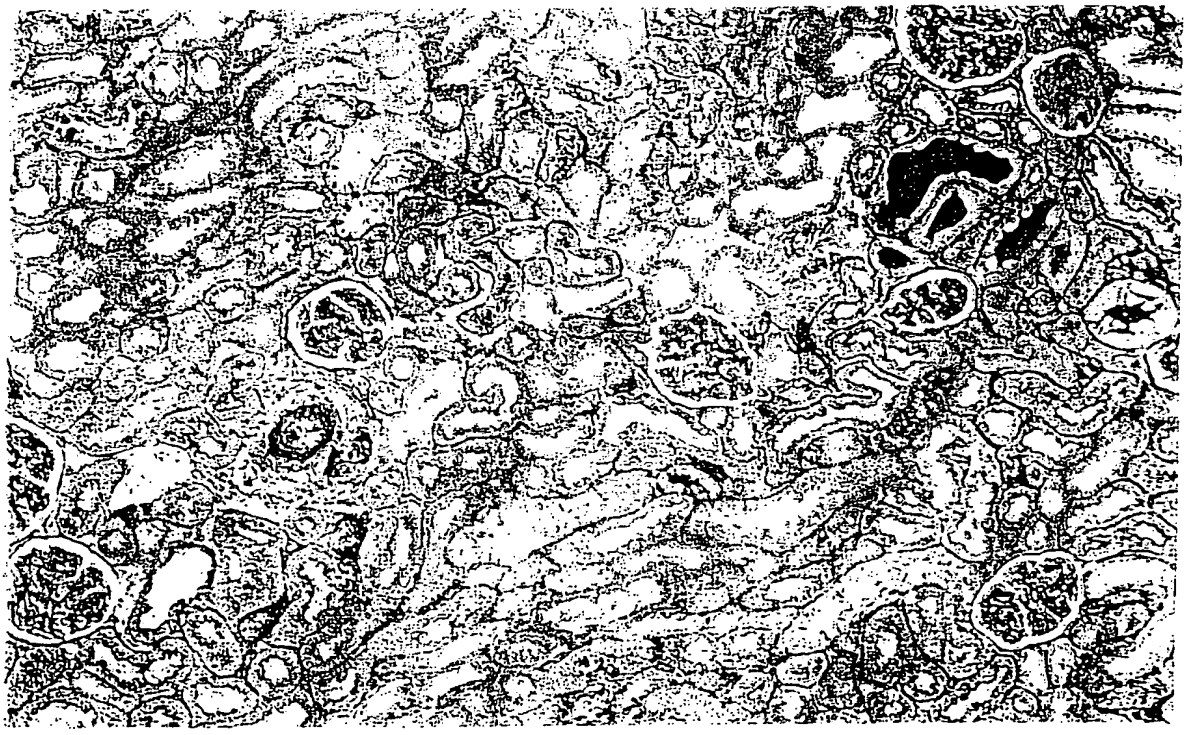


FIGURE A-6

C



D



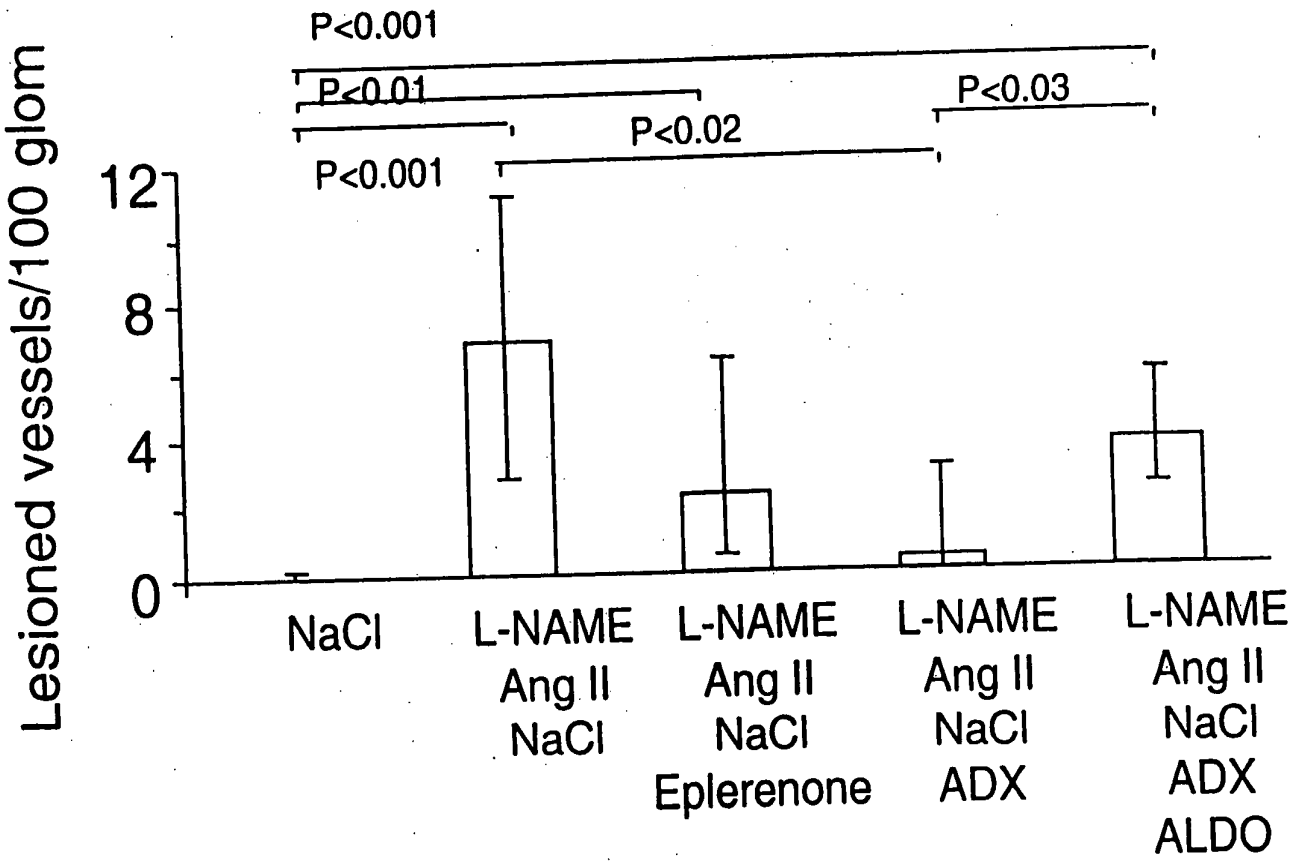
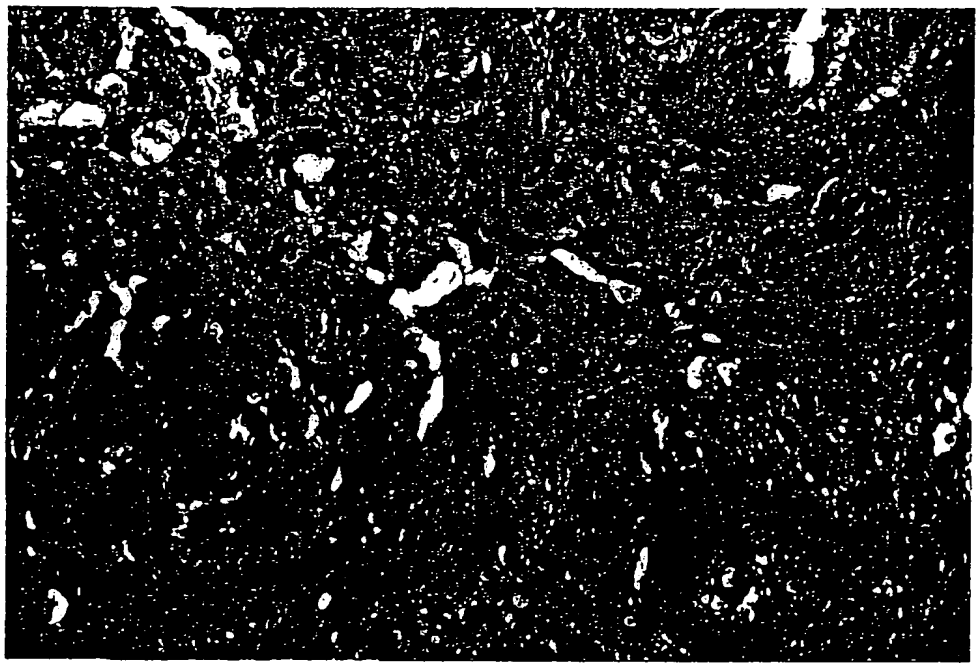


Figure A-7. Histopathologic scores for renal vascular injury.

100X



400X

Fig. A-8 INFLAMMATORY LESIONS IN CORONARY ARTERIES OF ALDOSTERONE/SALT UNINEPHRECTOMIZED RATS

Eplerenone-Treated Rat

100X

Fig. A-9 INFLAMMATORY LESIONS IN EPLERENONE-TREATED CORONARY ARTERIES OF ALDOSTERONE/SALT UNINEPHRECTOMIZED RATS

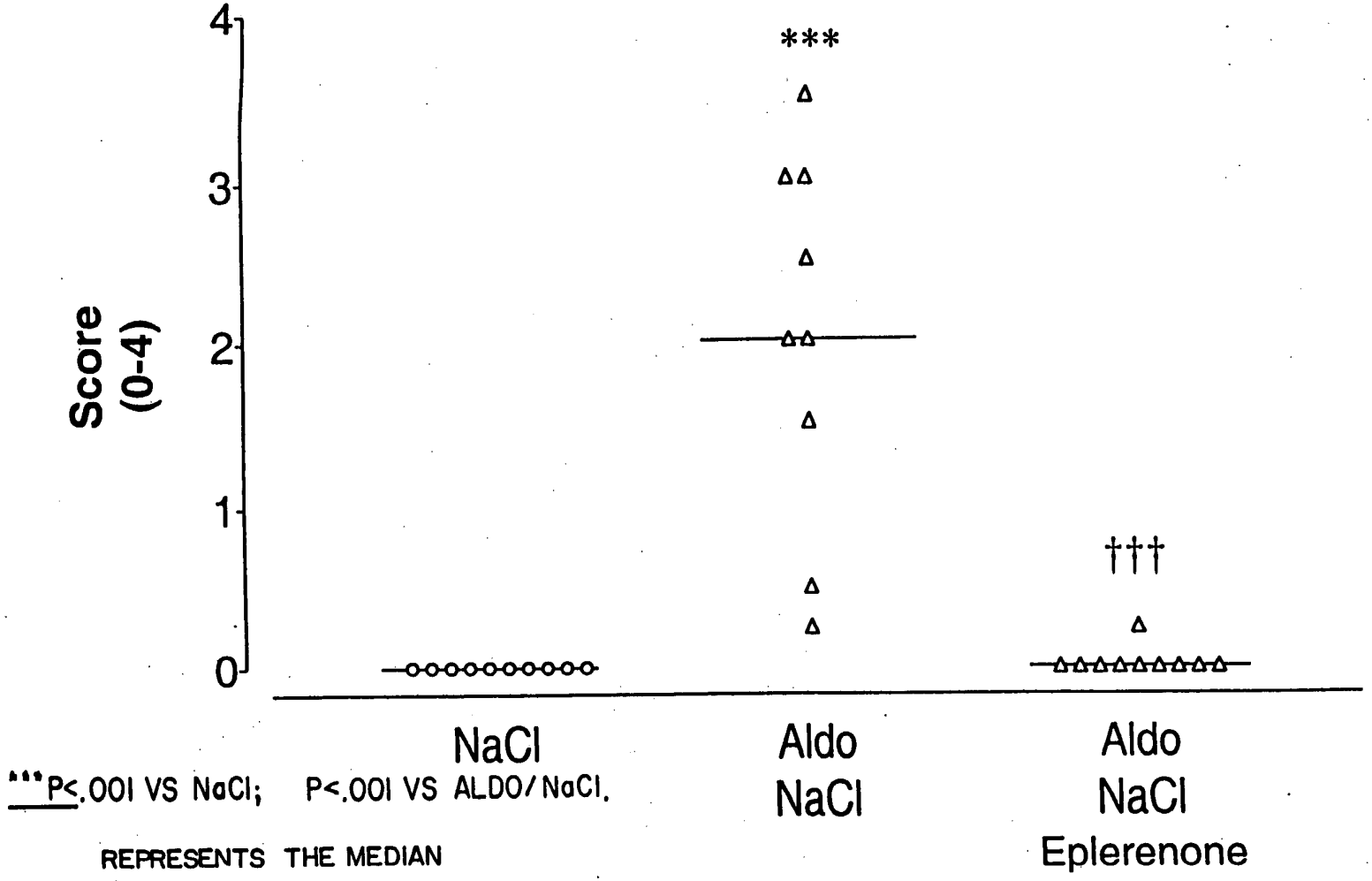


Fig. A-10: Myocardial Injury in Aldosterone/Salt Uninephrectomized Rats

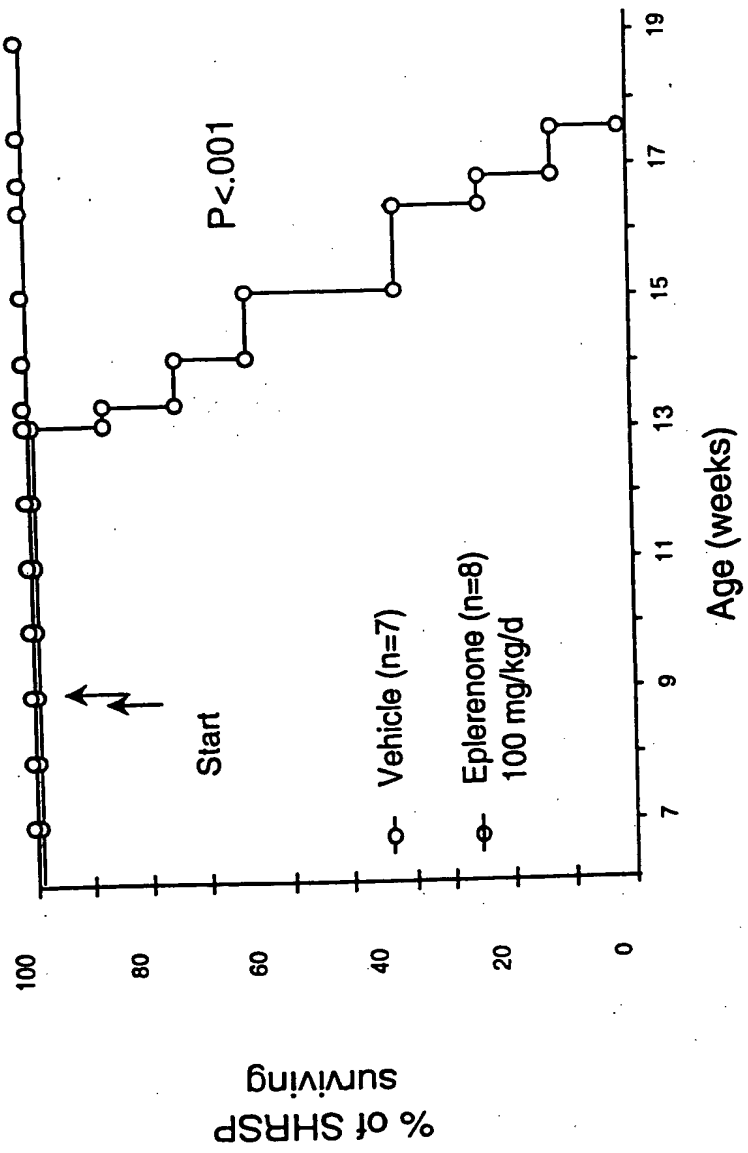


Fig. A-11: Survival in Saline-Drinking Stroke-Prone SHR Rats

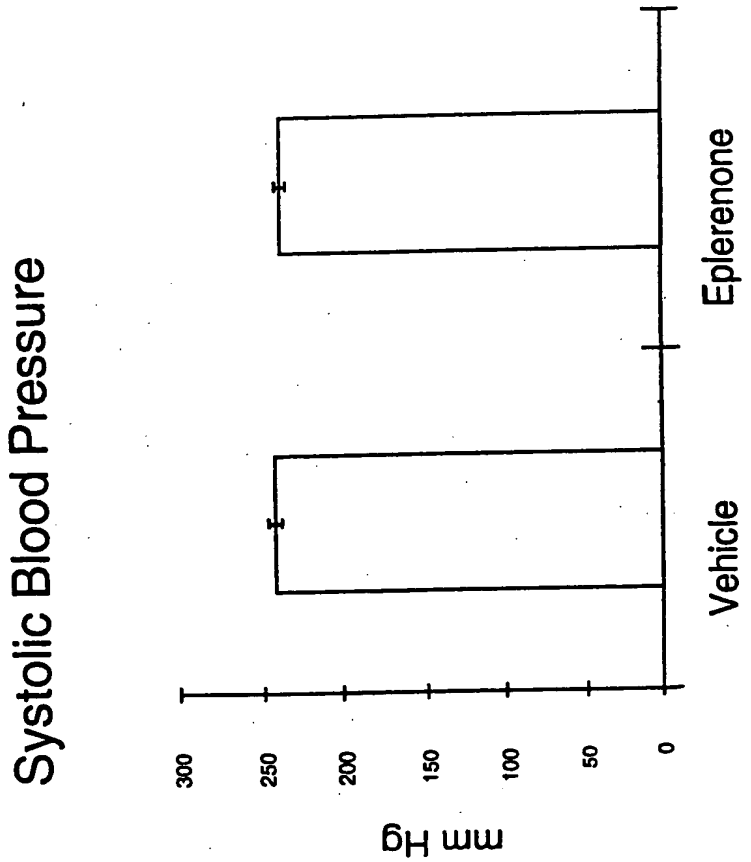
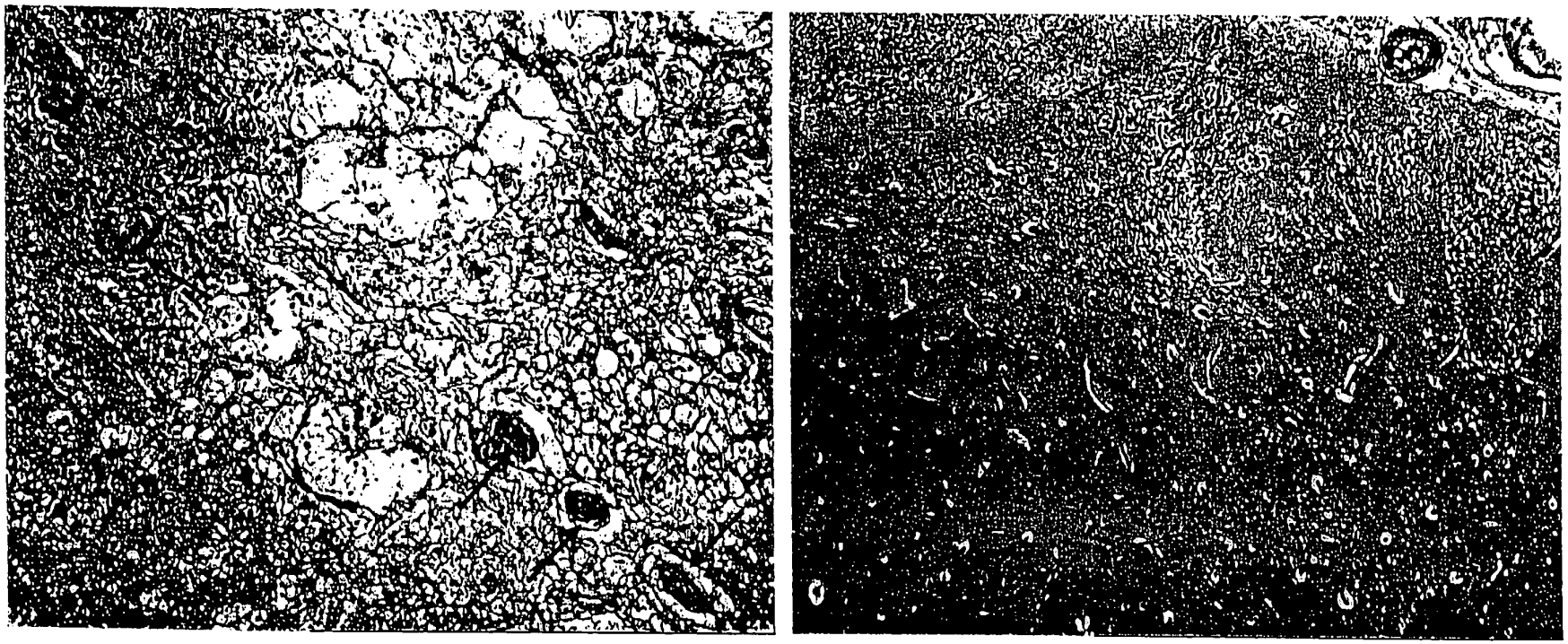


Fig. A-12: SBP in Saline-Drinking Stroke-Prone SHR Rats



Vehicle-Treated
SHRSP

Eplerenone-Treated
SHRSP

Fig. A-13: Cerebral Injury in Saline-Drinking Stroke-Prone SHR Rats

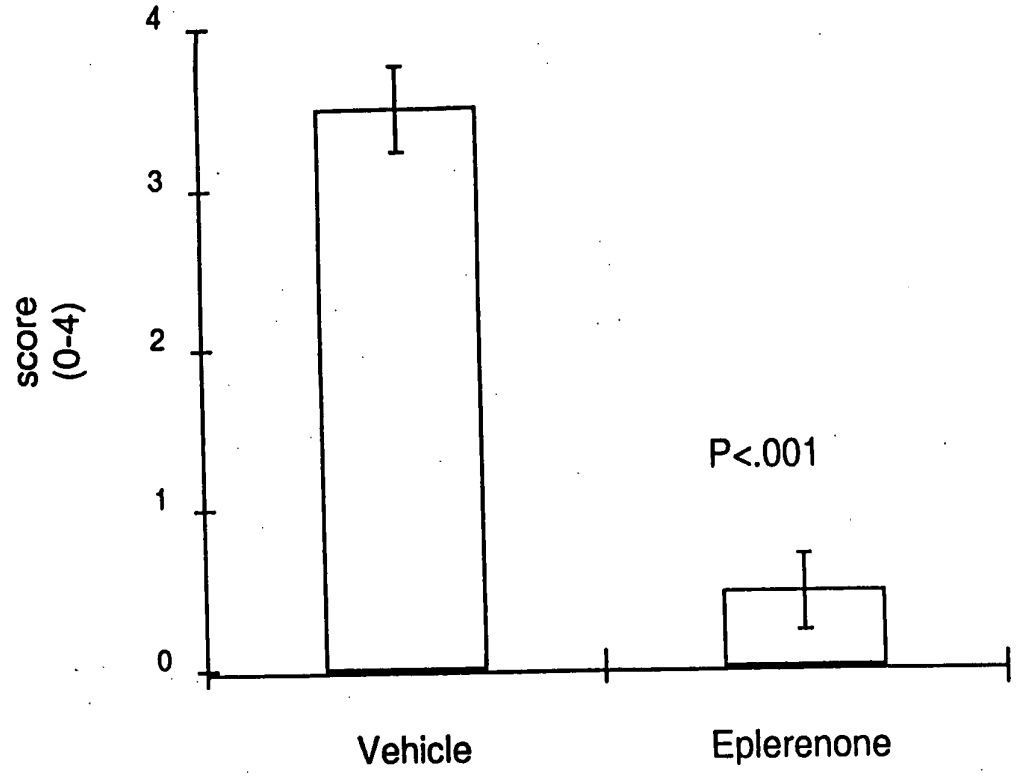


Fig. A-14: Cerebral Injury in Saline-Drinking Stroke-Prone SHR Rats

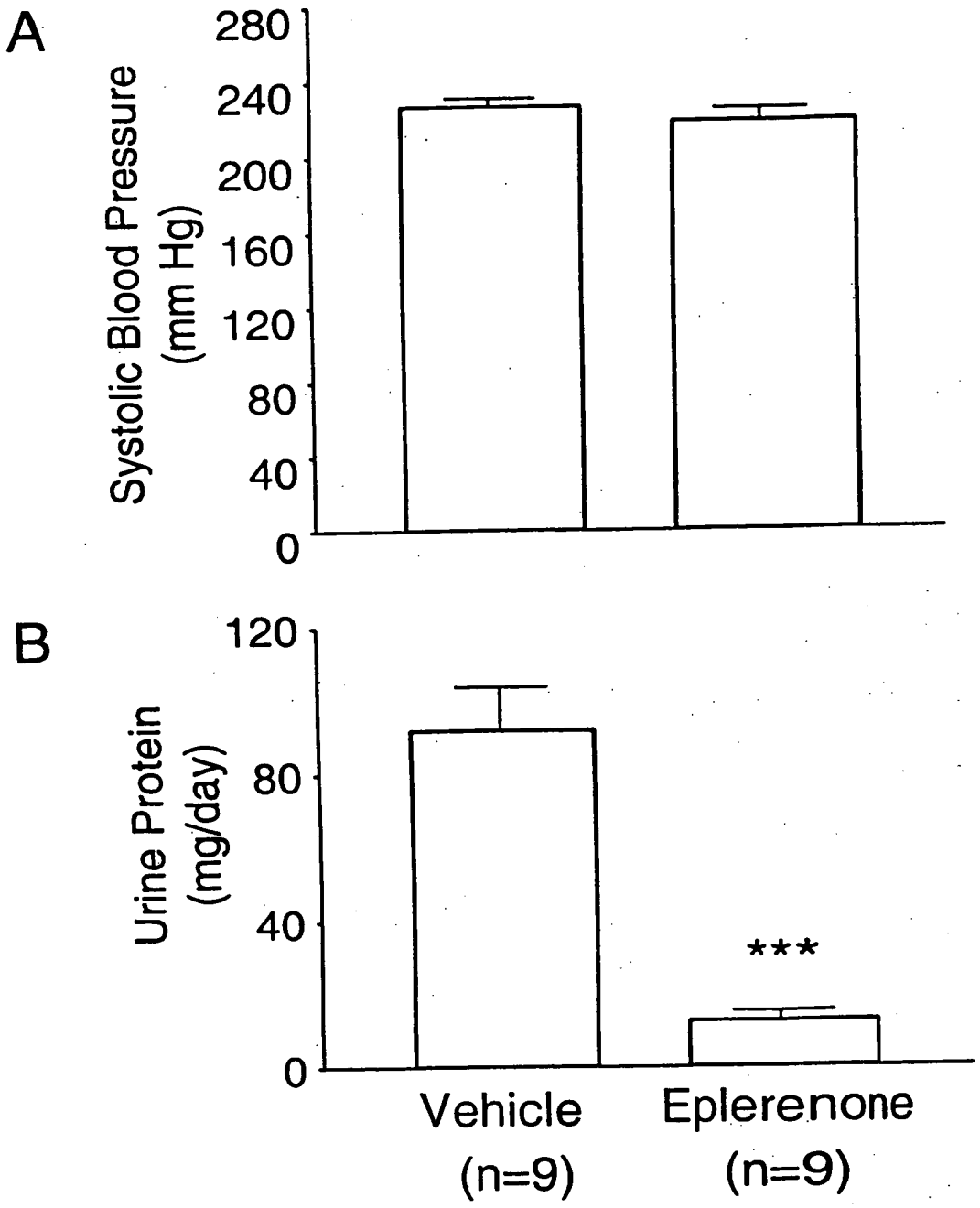
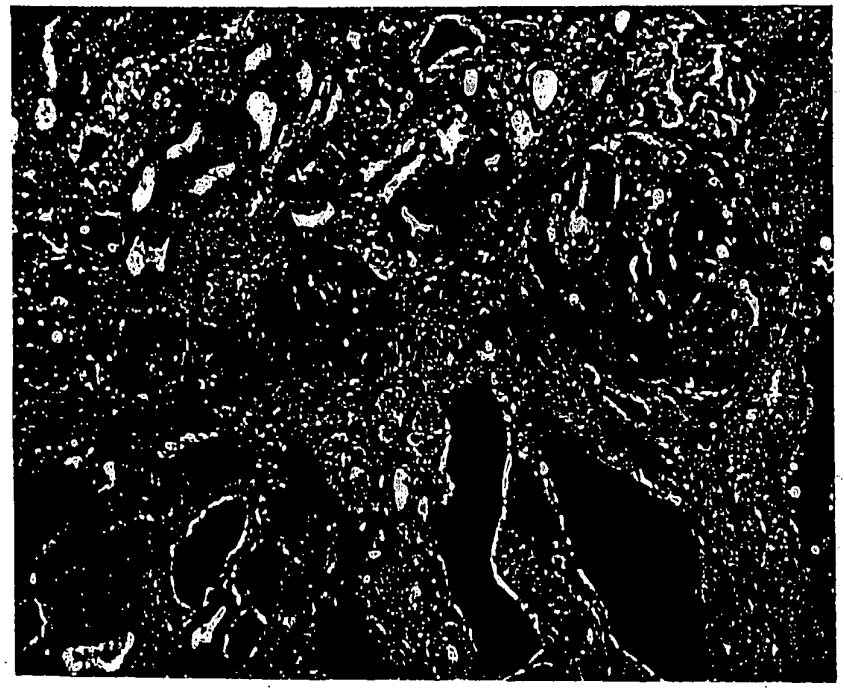

A
Systolic Blood Pressure (mm Hg)
280
240
200
160
120
80
40
0
B
Urine Protein (mg/day)
120
80
40
0
***
Vehicle (n=9)
Eplerenone (n=9)

Fig. A-15

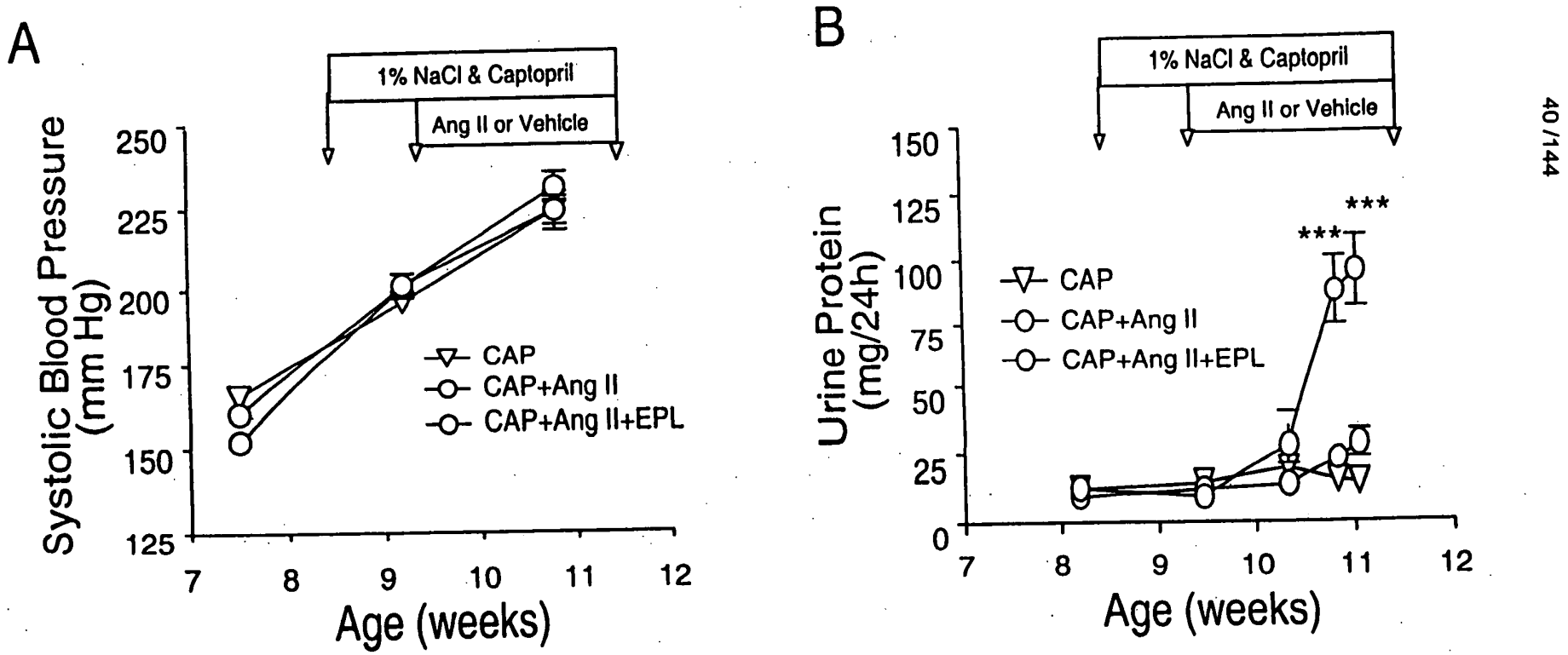
Fig. A-16



A

B

Fig. A-17


A
1% NaCl & Captopril
Ang II or Vehicle
Systolic Blood Pressure (mm Hg)
250
225
200
175
150
125
7
8
9
10
11
12
Age (weeks)
CAP
CAP+Ang II
CAP+Ang II+EPL
B
1% NaCl & Captopril
Ang II or Vehicle
Urine Protein (mg/24h)
150
125
100
75
50
25
0
***
***
CAP
CAP+Ang II
CAP+Ang II+EPL
7
8
9
10
11
12
Age (weeks)

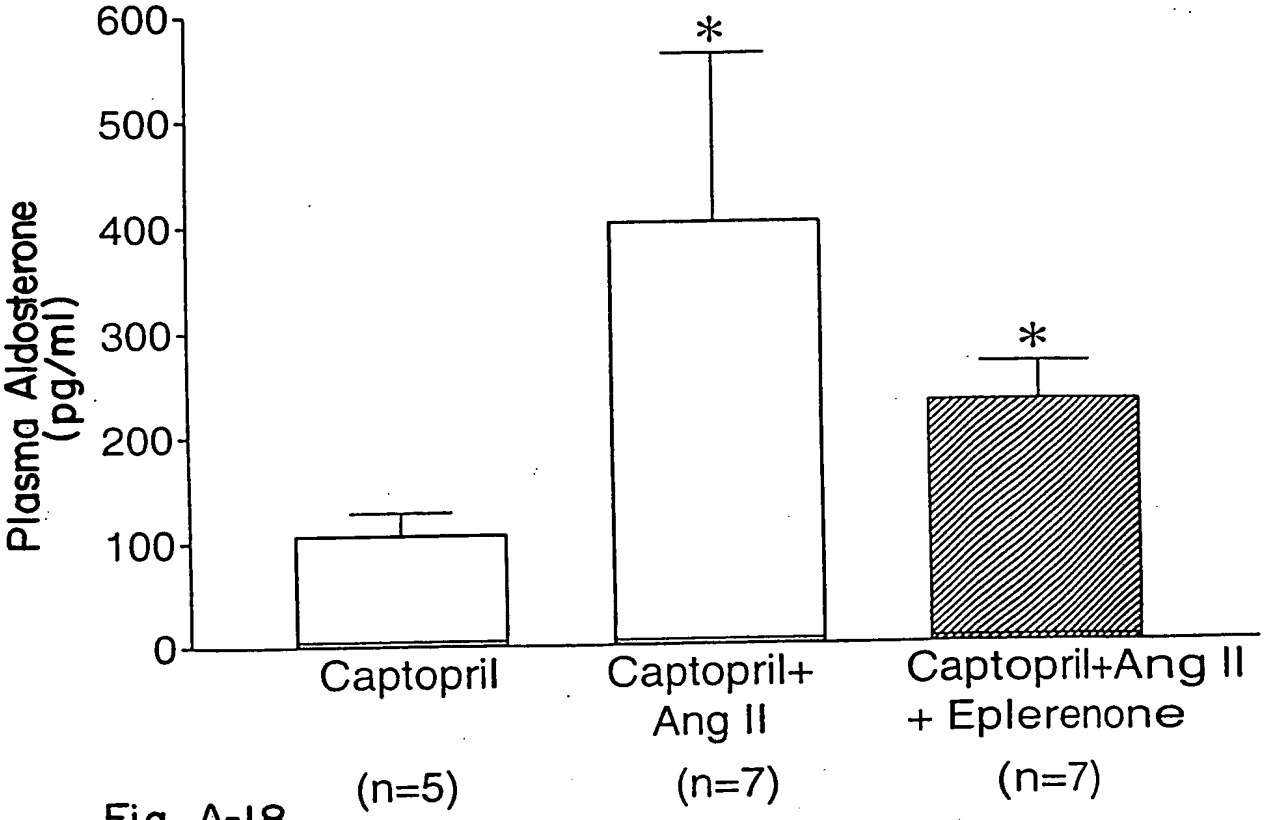


Fig. A-18

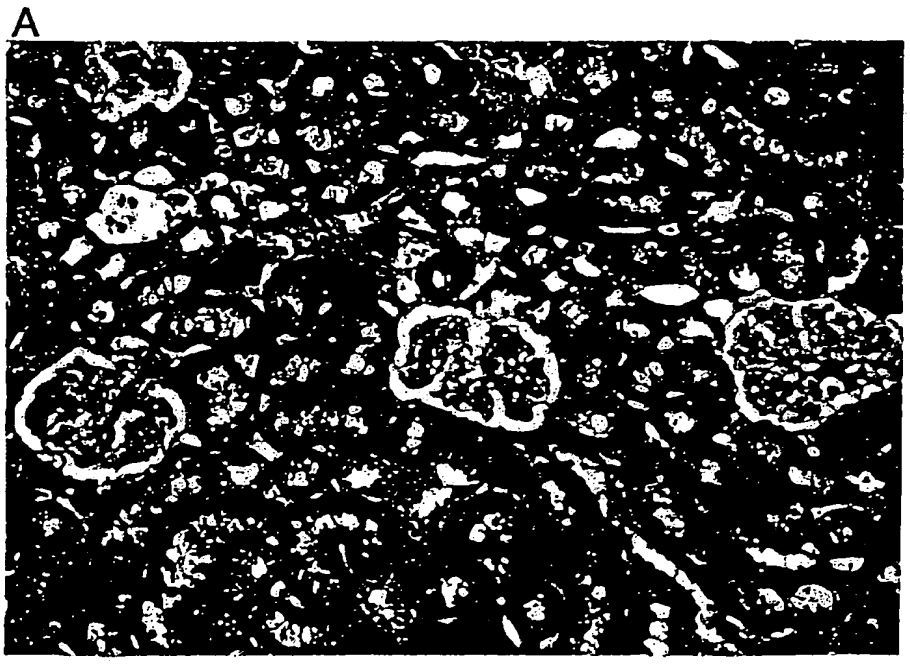


Fig. A-19

B

C

Fig. A-19 Cont'd.

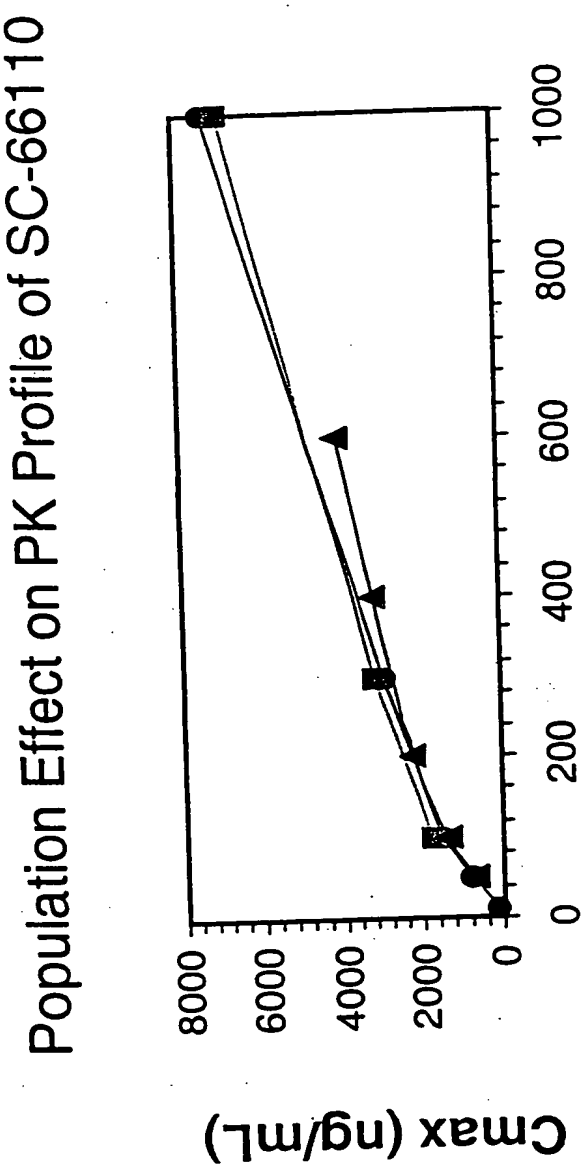

Population Effect on PK Profile of SC-66110
Cmax (ng/mL)
8000
6000
4000
2000
0
0
200
400
600
800
1000
DOSE (mg)

Figure A-20

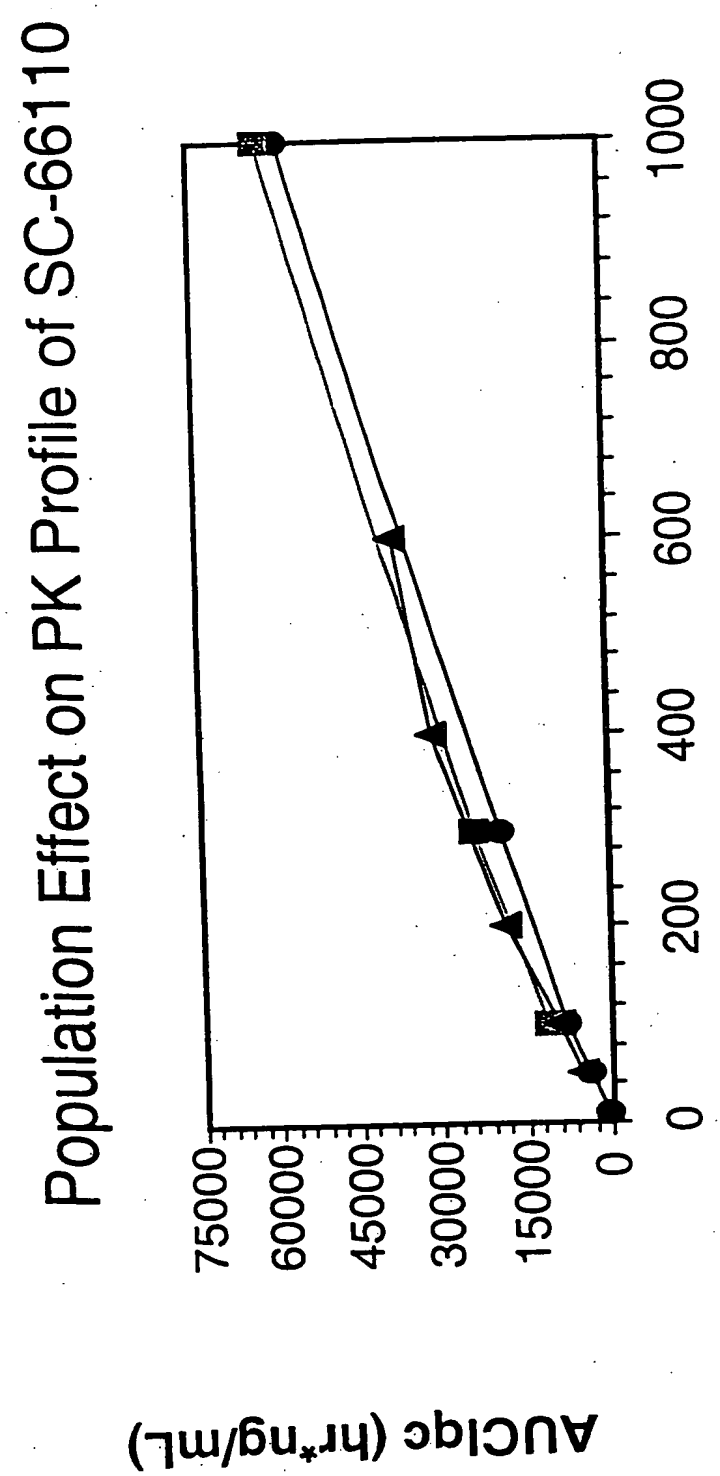

Population Effect on PK Profile of SC-66110
AUCIqc (hr*ng/mL)
75000
60000
45000
30000
15000
0
0
200
400
600
800
1000
DOSE (mg)

Figure A-21

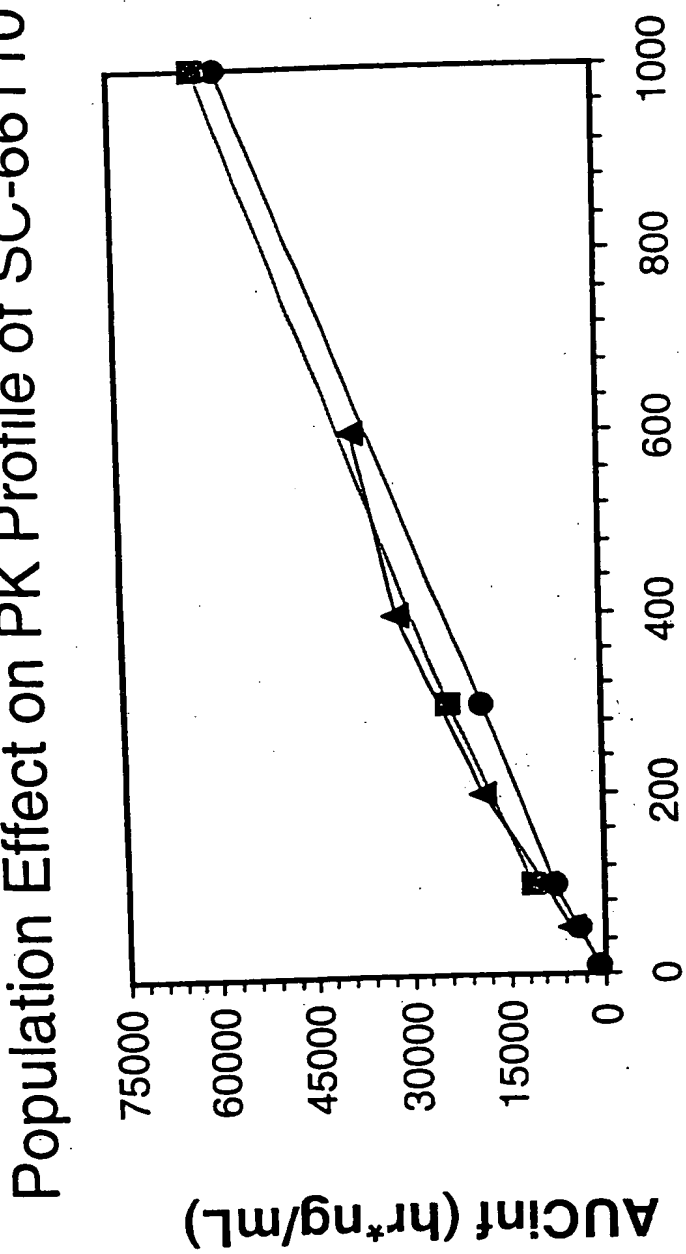

Population Effect on PK Profile of SC-66110
AUCinf (hr*ng/mL)
75000
60000
45000
30000
15000
0
0
200
400
600
800
1000
DOSE (mg)

Figure A-22

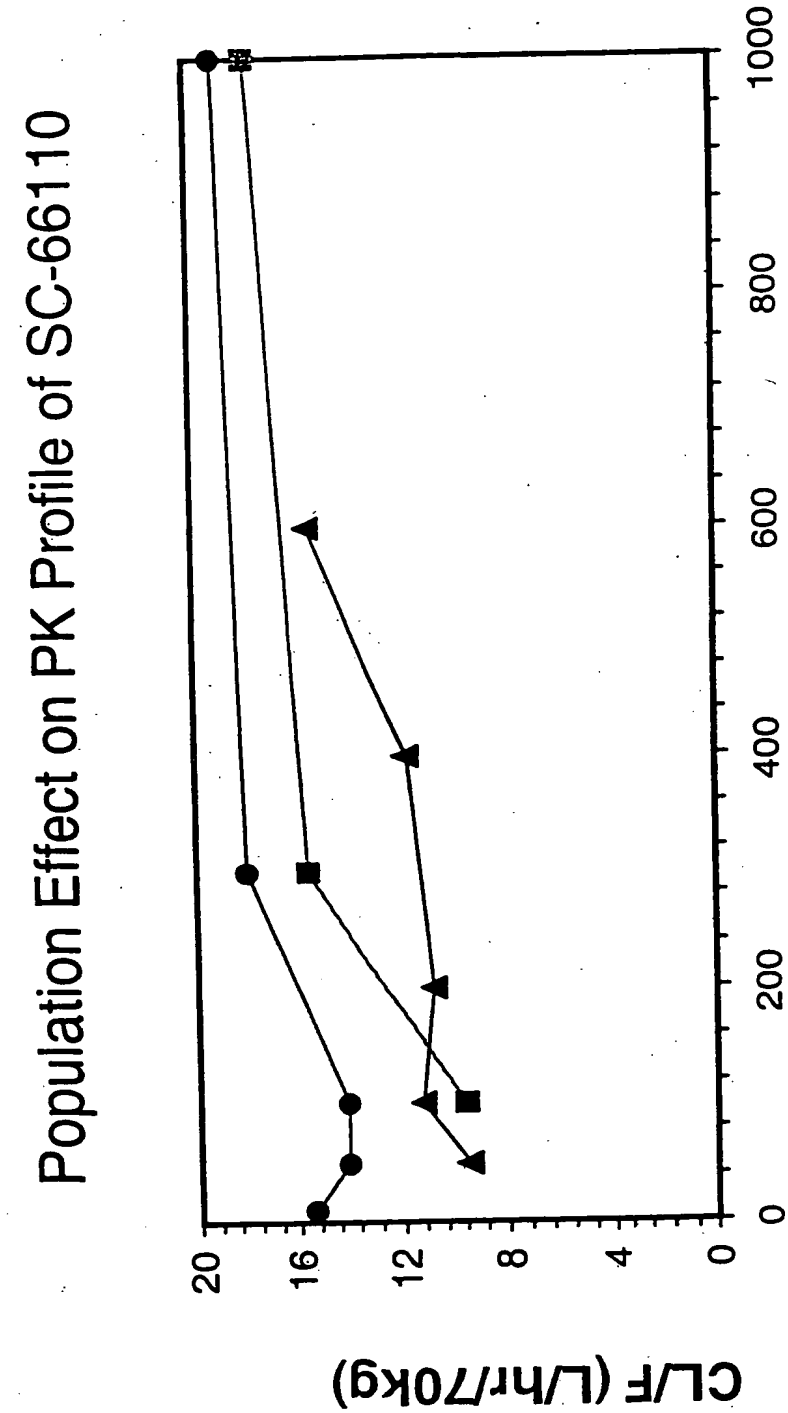

Population Effect on PK Profile of SC-66110
CL/F (L/hr/70kg)
20
16
12
8
4
0
0
200
400
600
800
1000
DOSE (mg)

Figure A-23

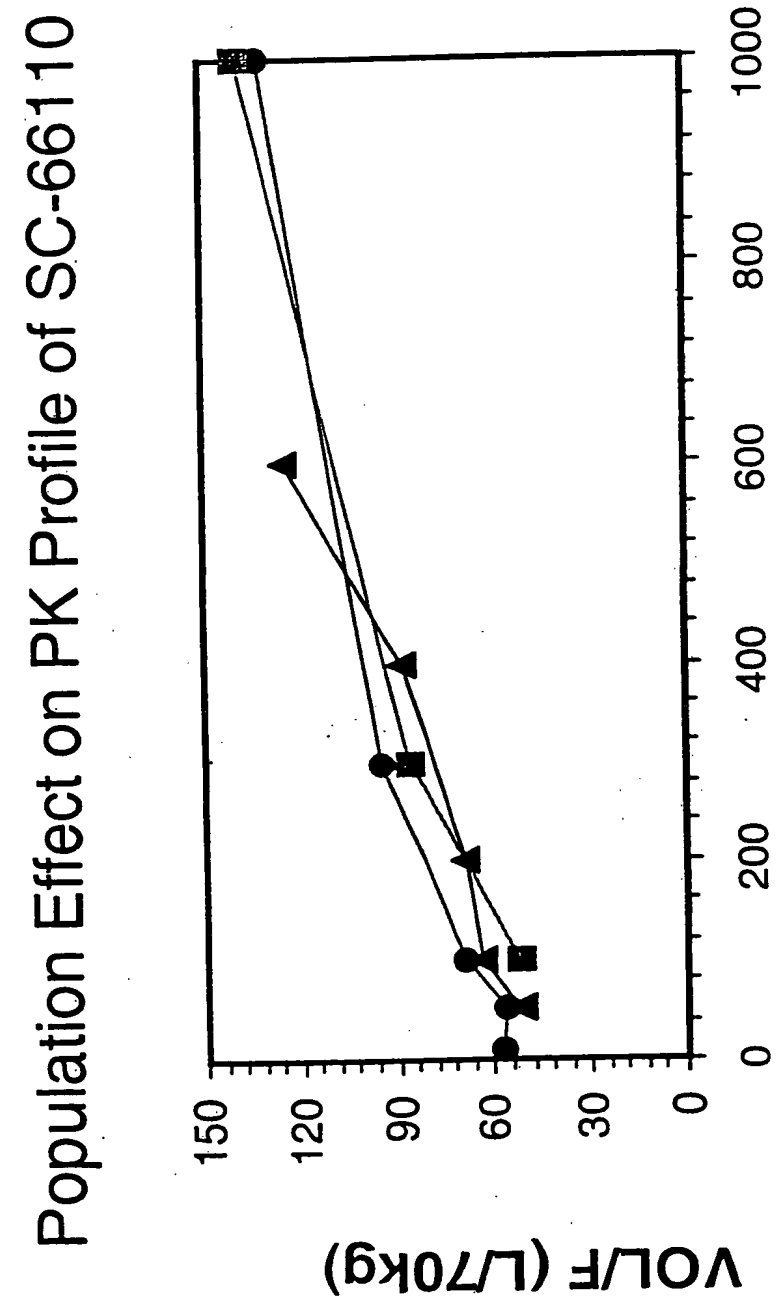

Population Effect on PK Profile of SC-66110
VOL/F (L/70kg)
150
120
90
60
30
0
0
200
400
600
800
1000
DOSE (mg)

Figure A-24

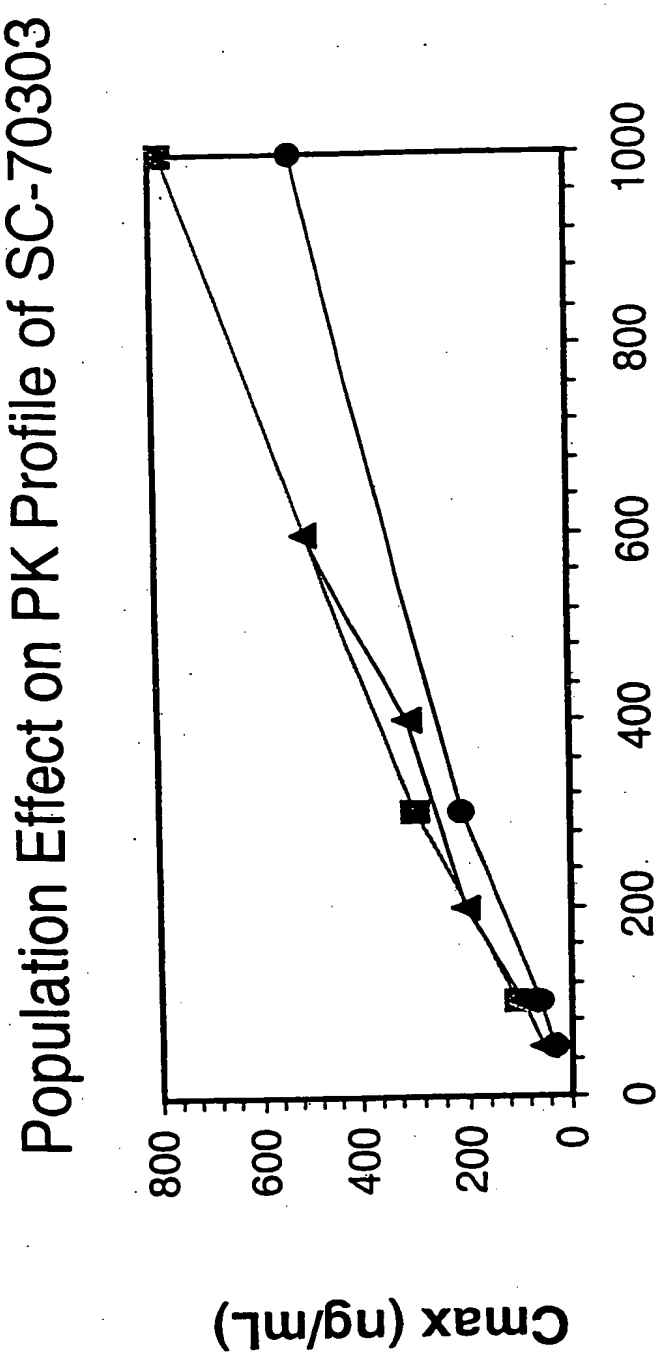

Population Effect on PK Profile of SC-70303
Cmax (ng/mL)
800
600
400
200
0
0
200
400
600
800
1000
DOSE (mg)

Figure A-25

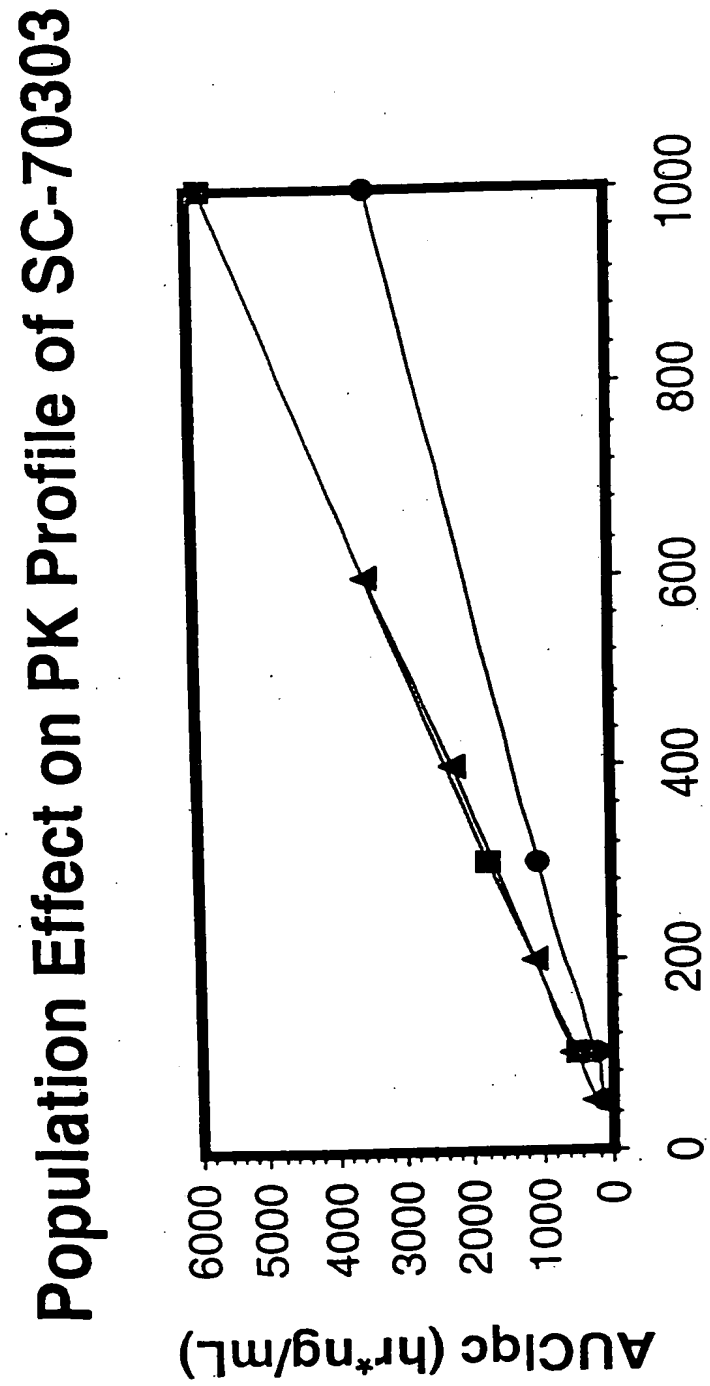

Population Effect on PK Profile of SC-70303
AUCIdc (hr*ng/mL)
6000
5000
4000
3000
2000
1000
0
0
200
400
600
800
1000
DOSE (mg)

Figure A-26

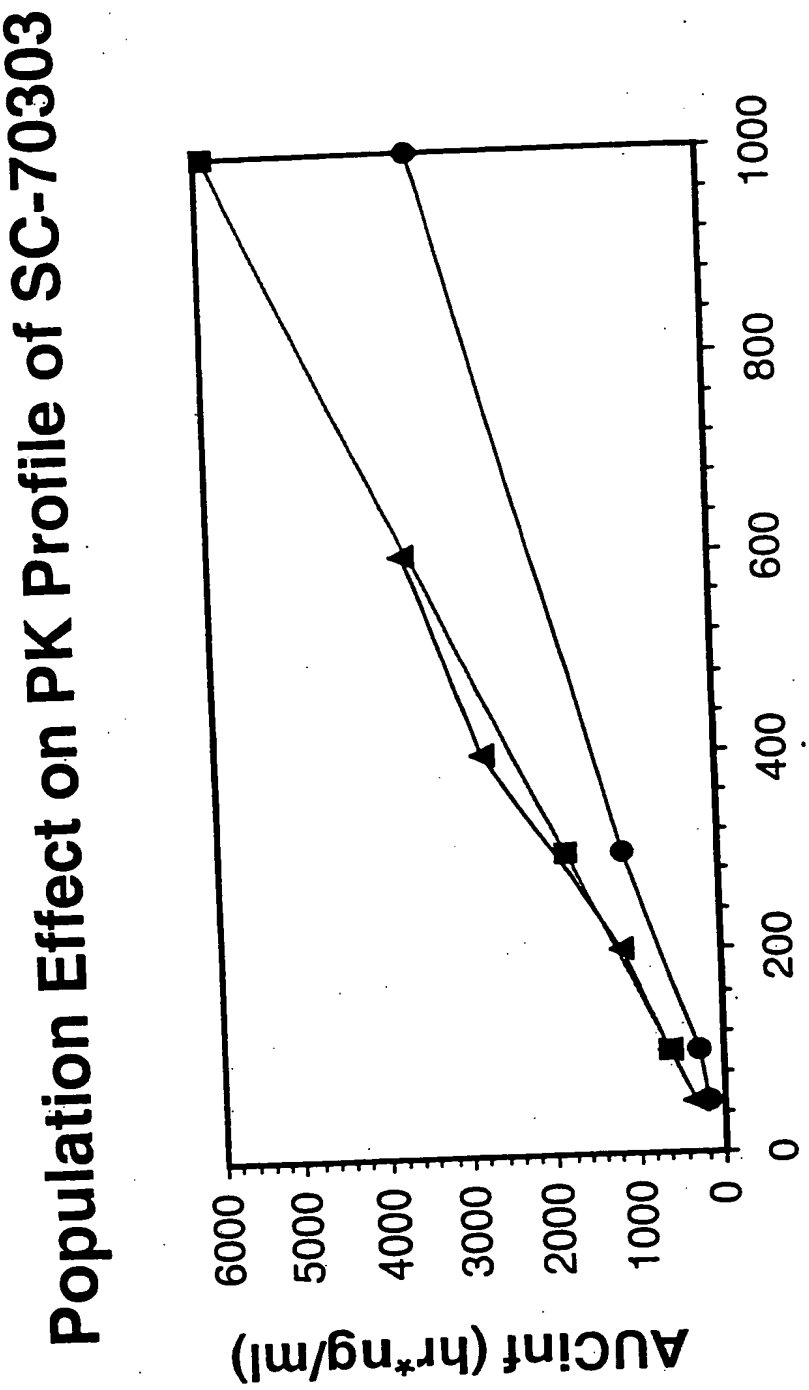

Population Effect on PK Profile of SC-70303
AUCinf (hr*ng/ml)
6000
5000
4000
3000
2000
1000
0
0
200
400
600
800
1000
DOSE (mg)

Figure A-27

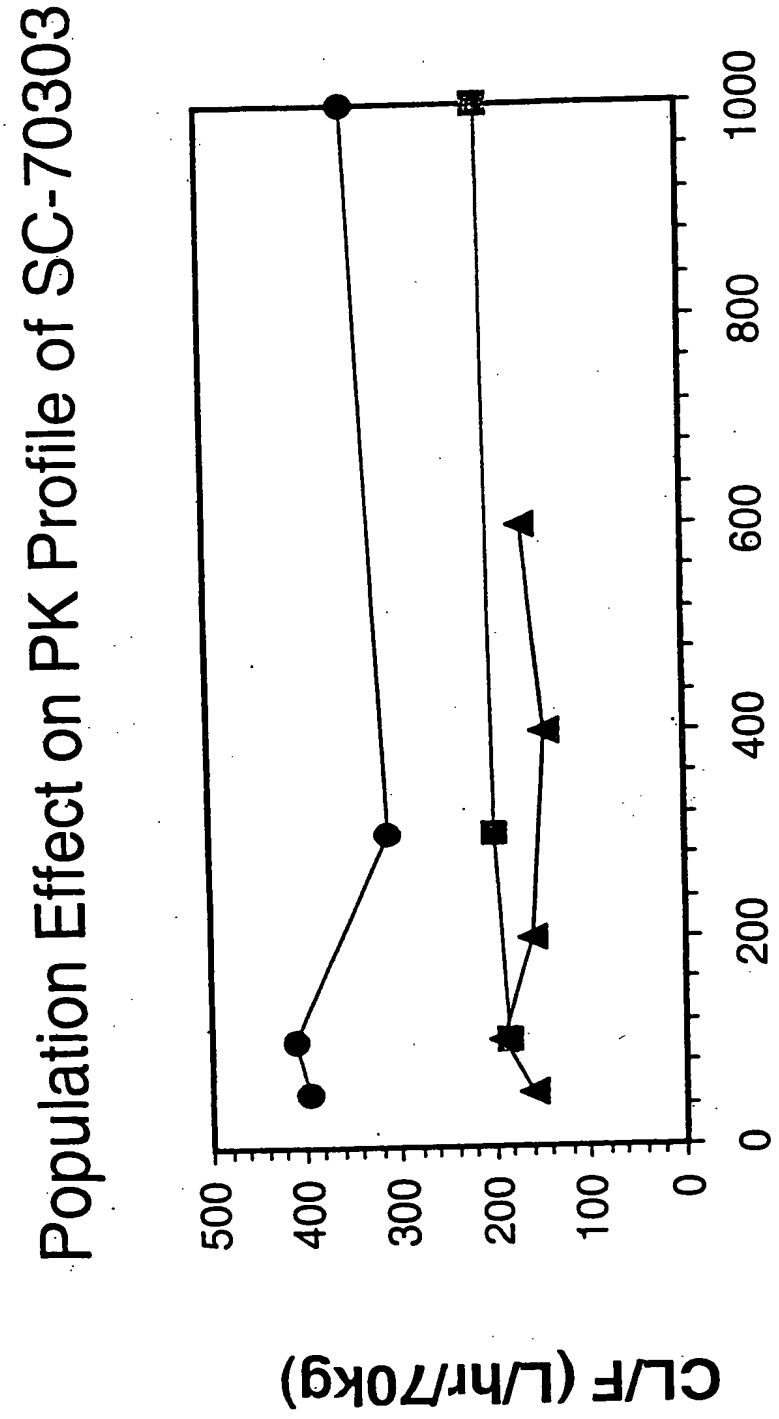

Population Effect on PK Profile of SC-70303
CL/F (L/hr/70kg)
500
400
300
200
100
0
0
200
400
600
800
1000
DOSE (mg)

Figure A-28

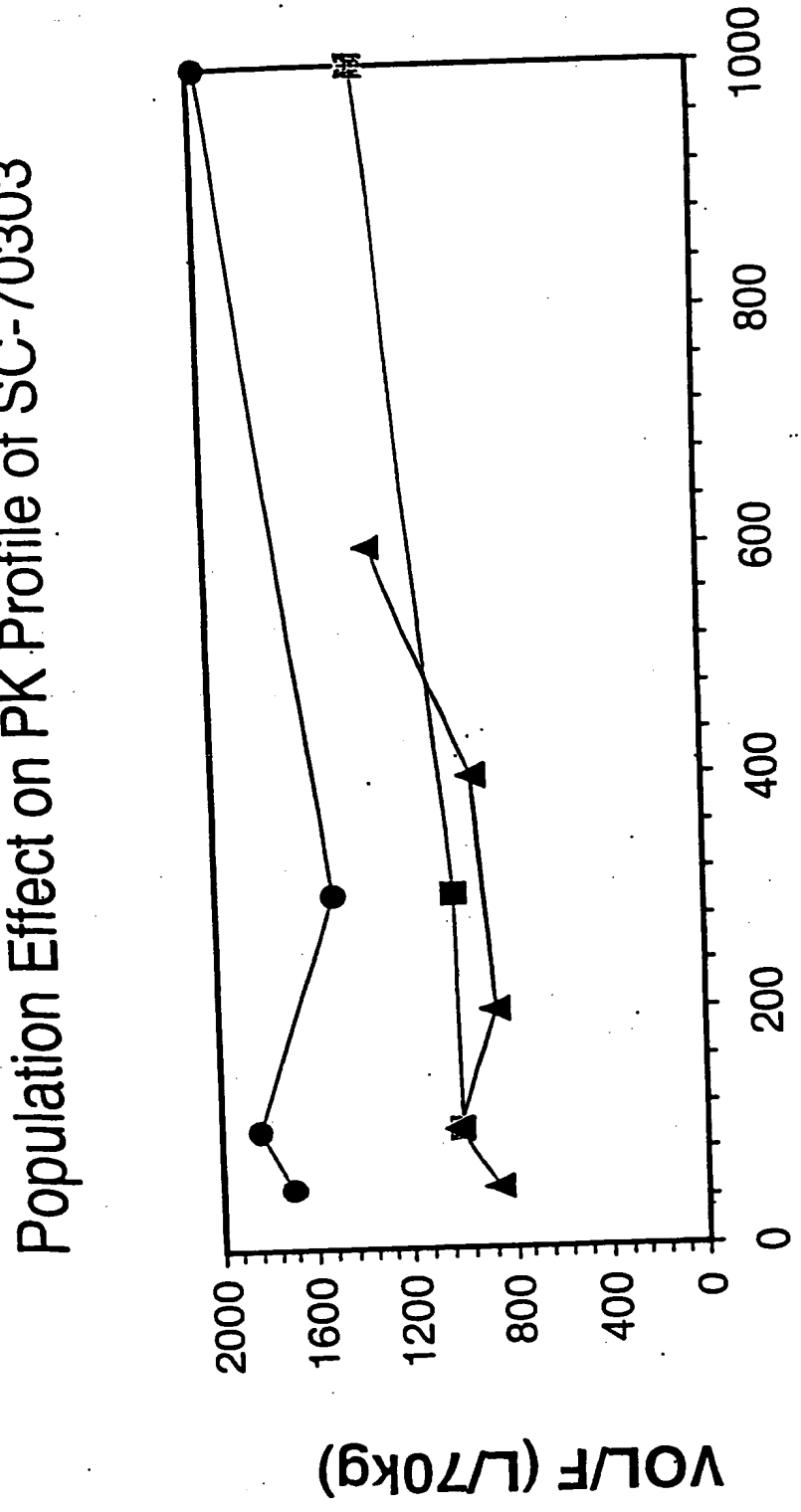

Population Effect on PK Profile of SC-70303
VOL/F (L/70kg)
2000
1600
1200
800
400
0
0
200
400
600
800
1000
DOSE (mg)

Figure A-29

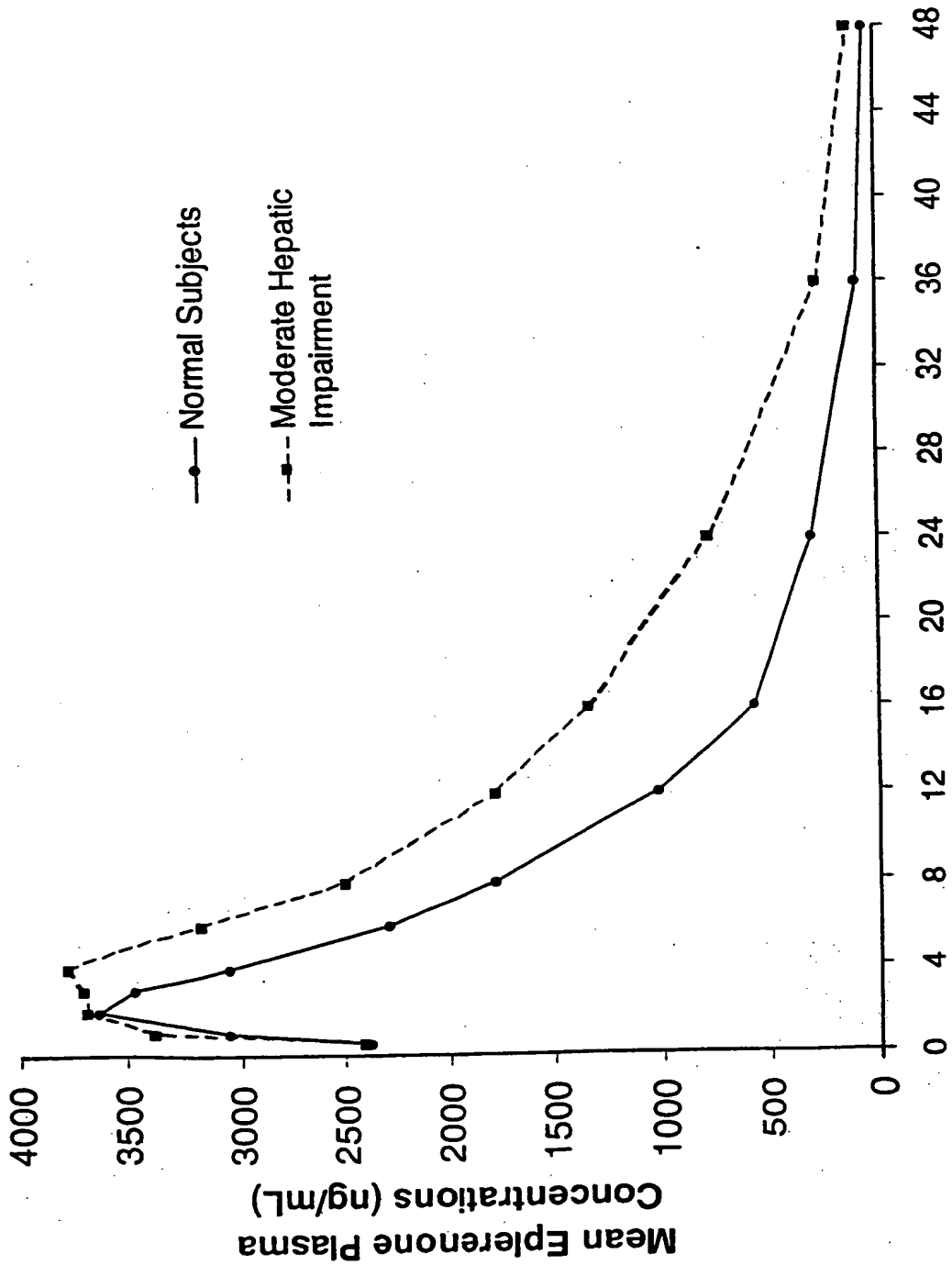

Mean Eplerenone Plasma Concentrations (ng/mL)
4000
3500
3000
2500
2000
1500
1000
500
0
0
4
8
12
16
20
24
28
32
36
40
44
48
Time (hr)
Normal Subjects
Moderate Hepatic Impairment

Figure A-30

FIGURE C-1

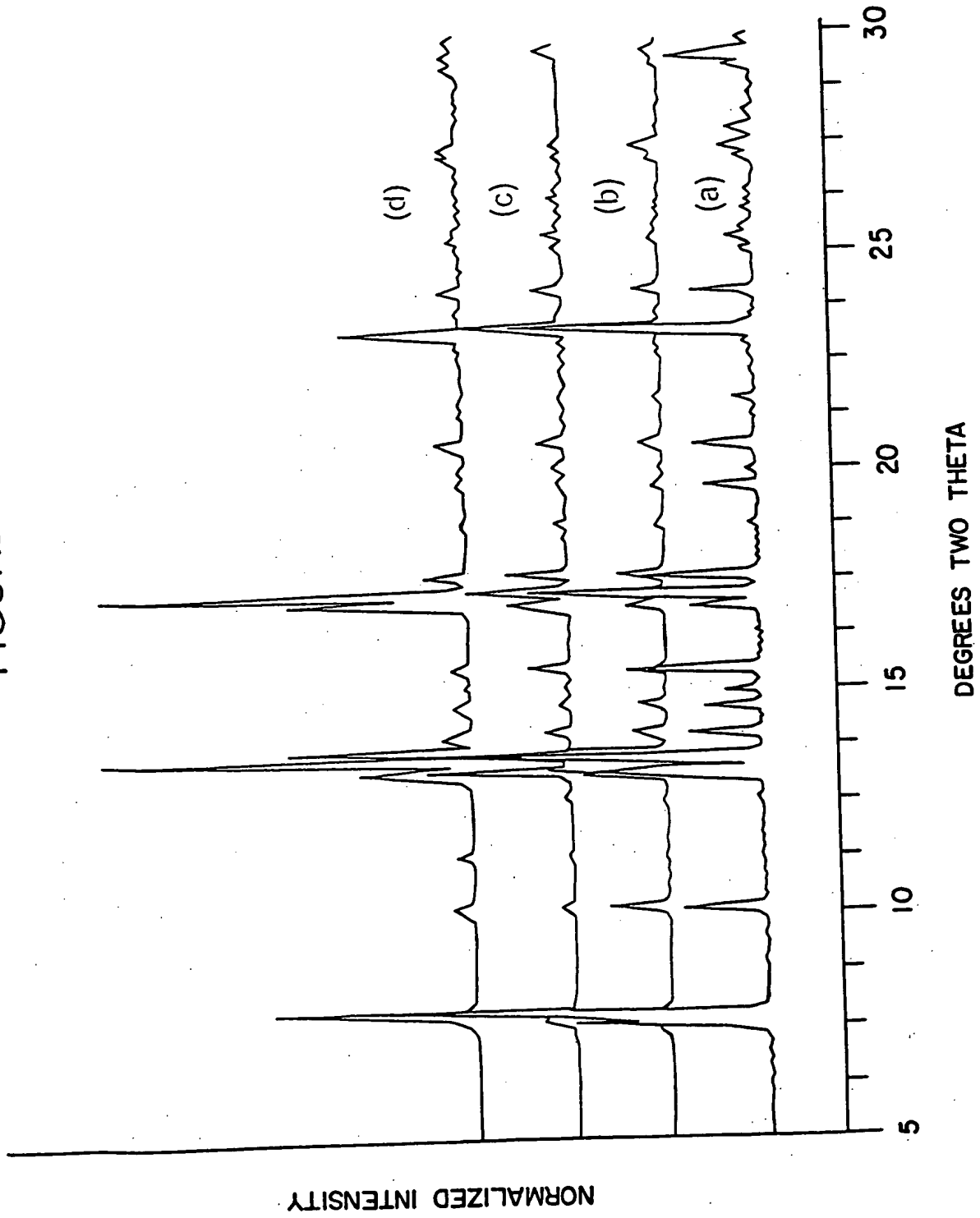


FIGURE C-2

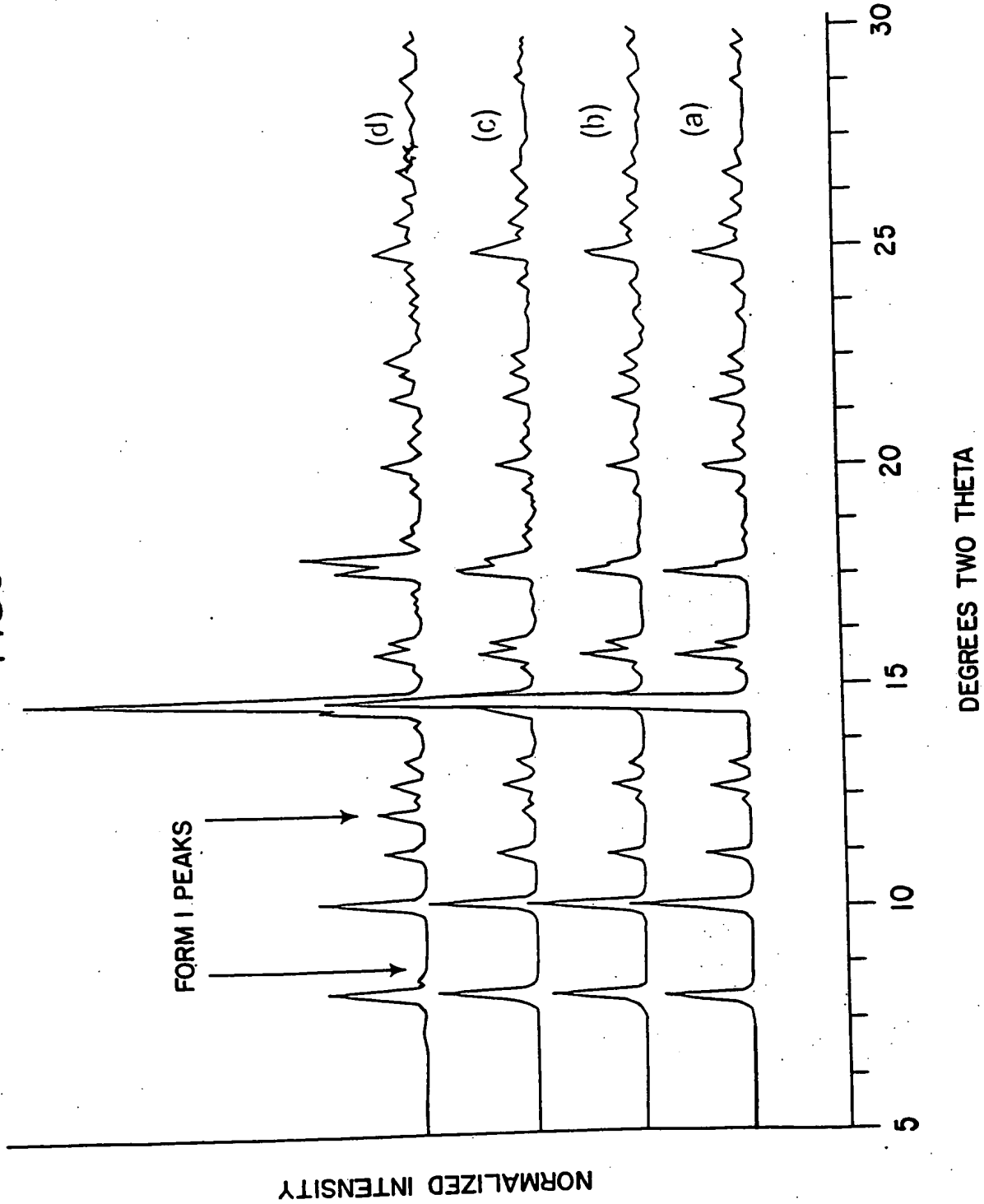

FORM I PEAKS
(d)
(c)
(b)
(a)
5
10
15
20
25
30
DEGREES TWO THETA
NORMALIZED INTENSITY

FIGURE C-3

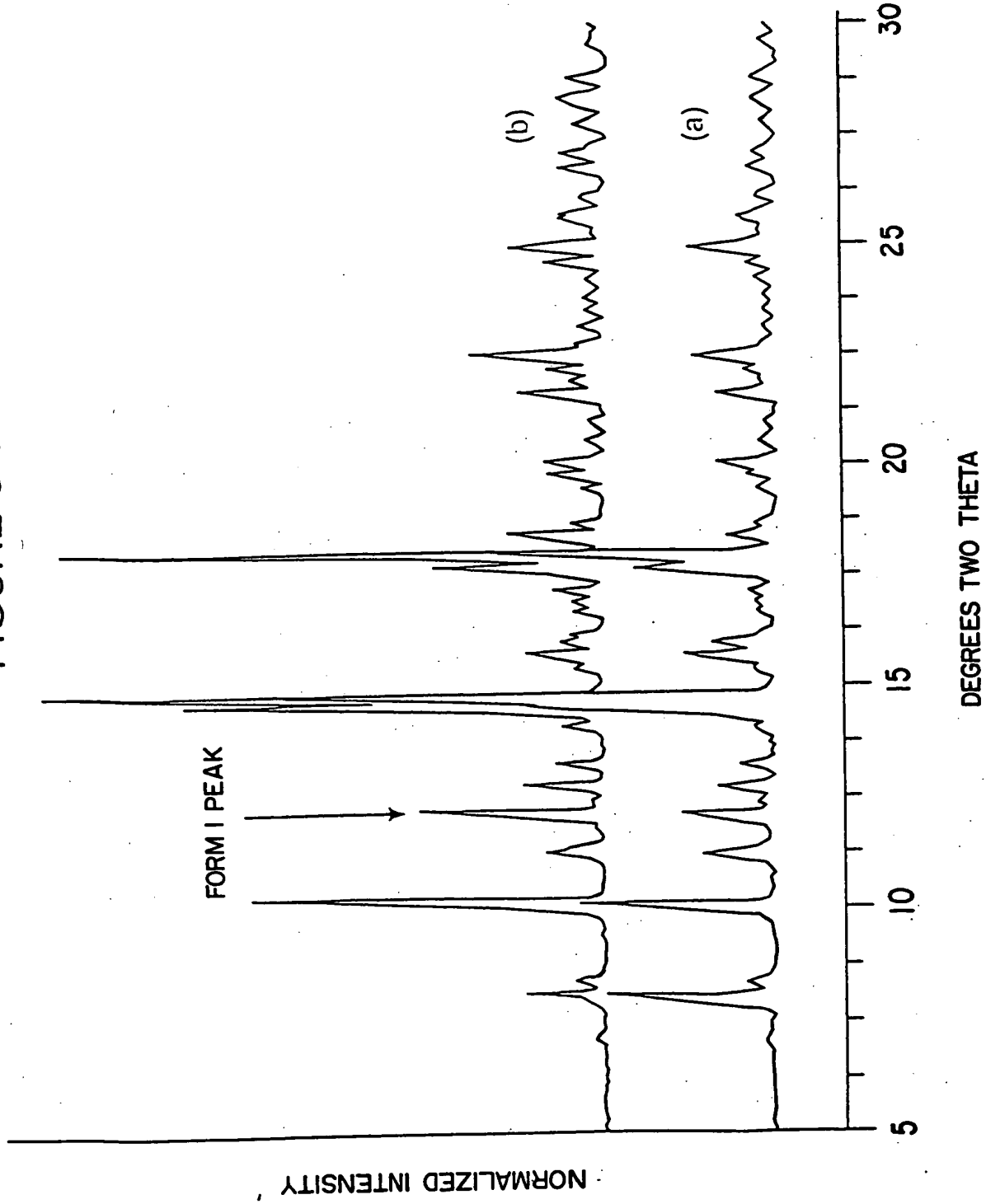

NORMALIZED INTENSITY
FORM I PEAK
(b)
(a)
5
10
15
20
25
30
DEGREES TWO THETA

FIGURE C-4

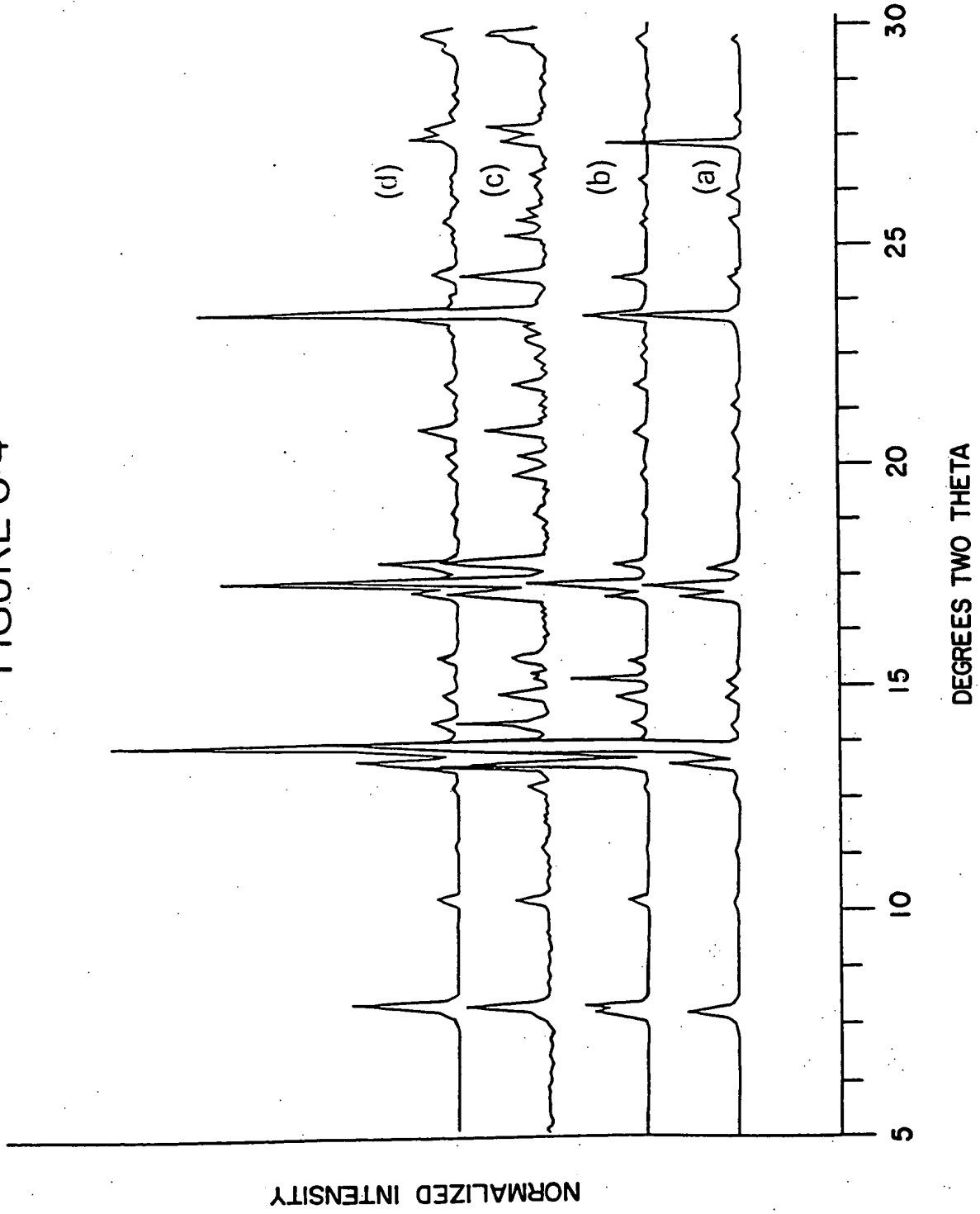


FIGURE C-5

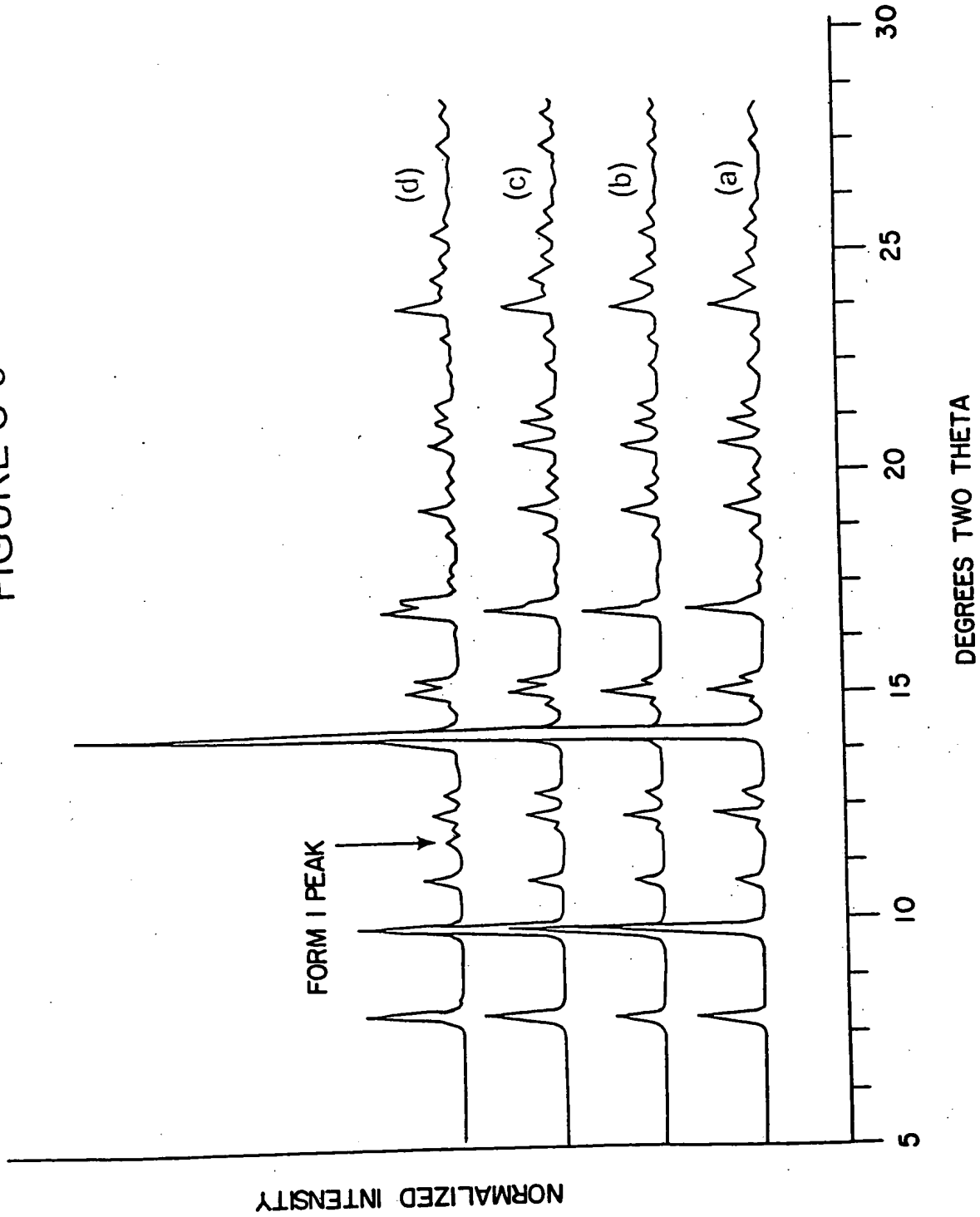

NORMALIZED INTENSITY
FORM I PEAK
(d)
(c)
(b)
(a)
5
10
15
20
25
30
DEGREES TWO THETA

Fig. C-6

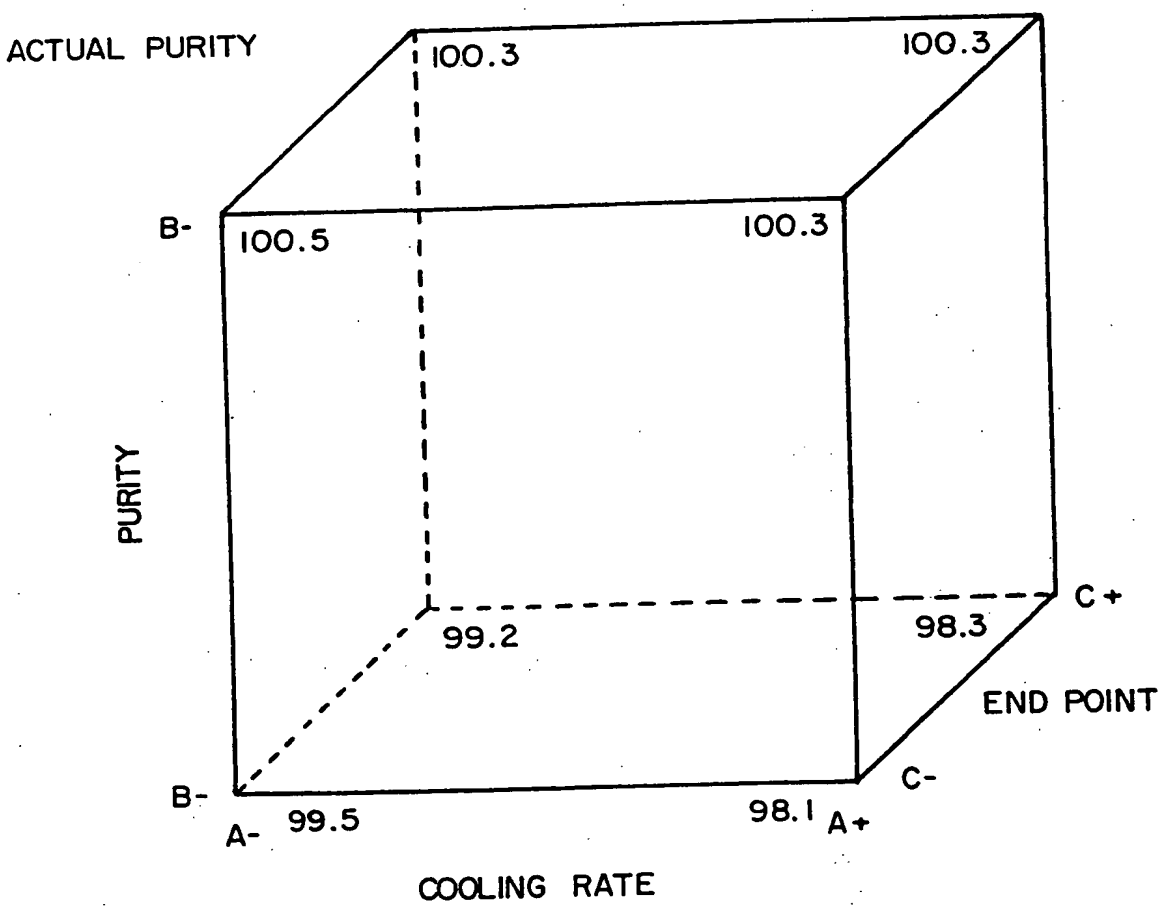

ACTUAL PURITY
100.3
100.3
B-
100.5
100.3
PURITY
99.2
98.3
C+
END POINT
B-
C-
A-
99.5
98.1
A+
COOLING RATE

Fig. C-7

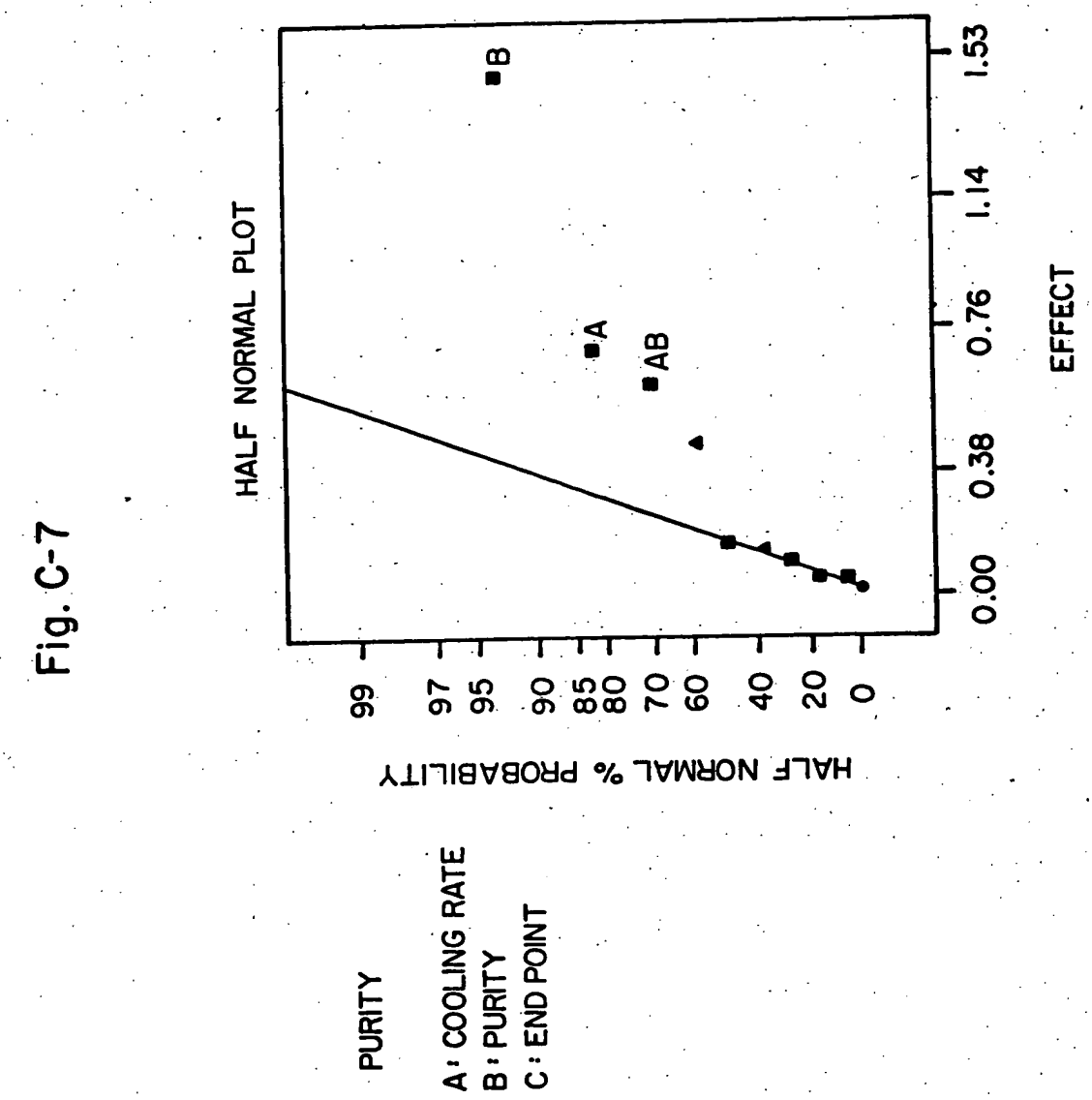

HALF NORMAL PLOT
HALF NORMAL % PROBABILITY
99
97
95
90
85
80
70
60
40
20
0
0.00
0.38
0.76
1.14
1.53
EFFECT
B
A
AB
PURITY
A: COOLING RATE
B: PURITY
C: END POINT

Fig. C-8

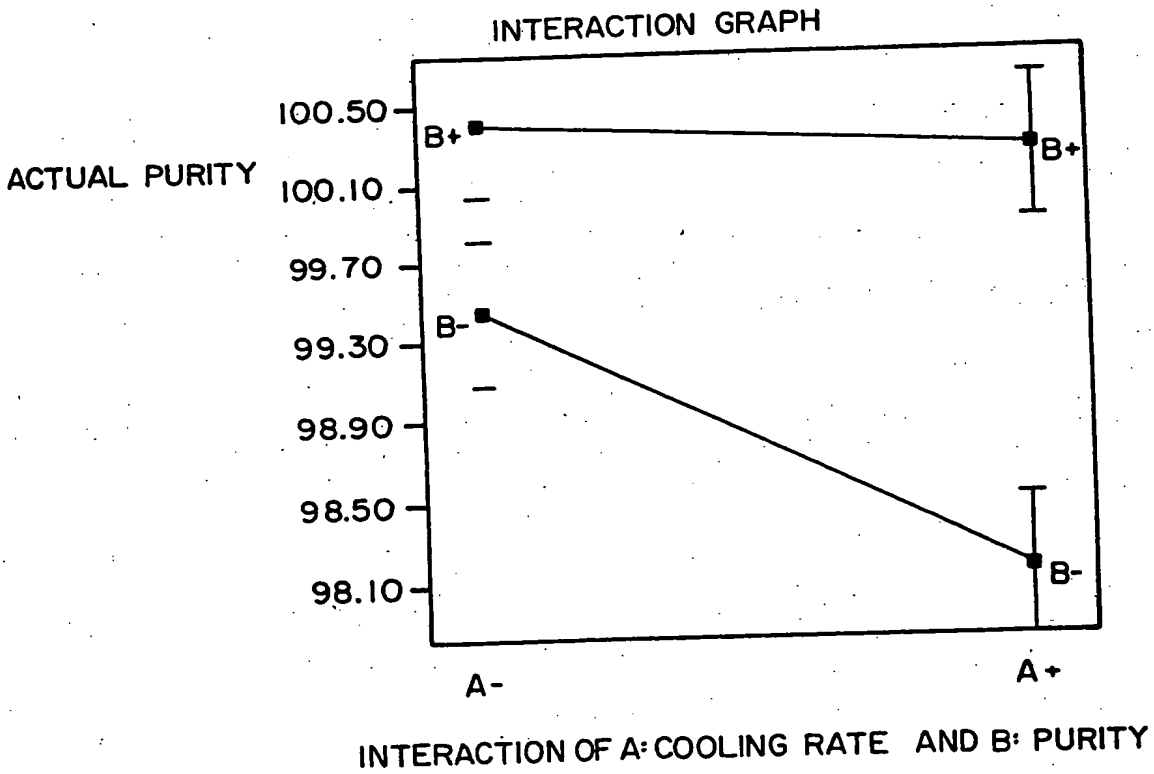
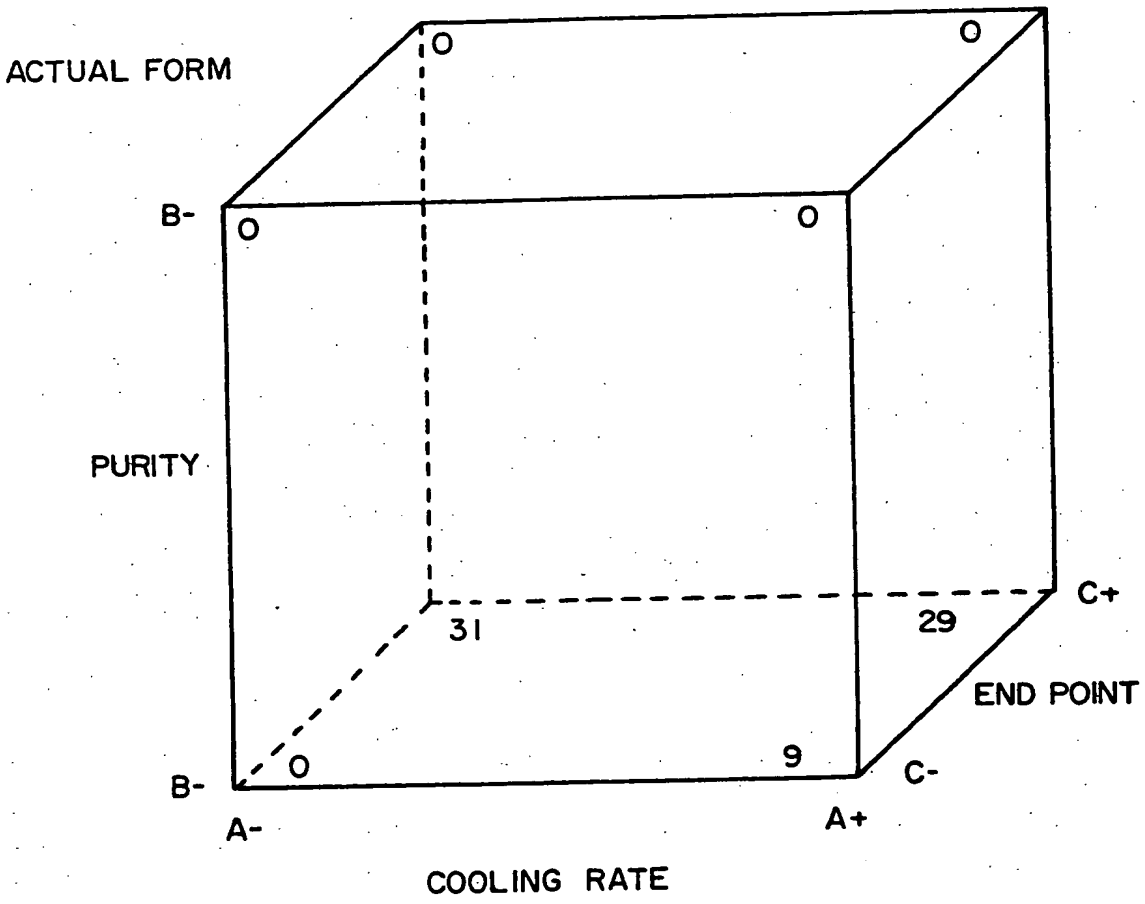

INTERACTION GRAPH
ACTUAL PURITY
100.50
100.10
99.70
99.30
98.90
98.50
98.10
B+
B+
B-
B-
A-
A+
INTERACTION OF A: COOLING RATE AND B: PURITY

Fig. C-9


ACTUAL FORM
O
O
B-
O
O
PURITY
31
29
C+
END POINT
B-
O
9
C-
A-
A+
COOLING RATE

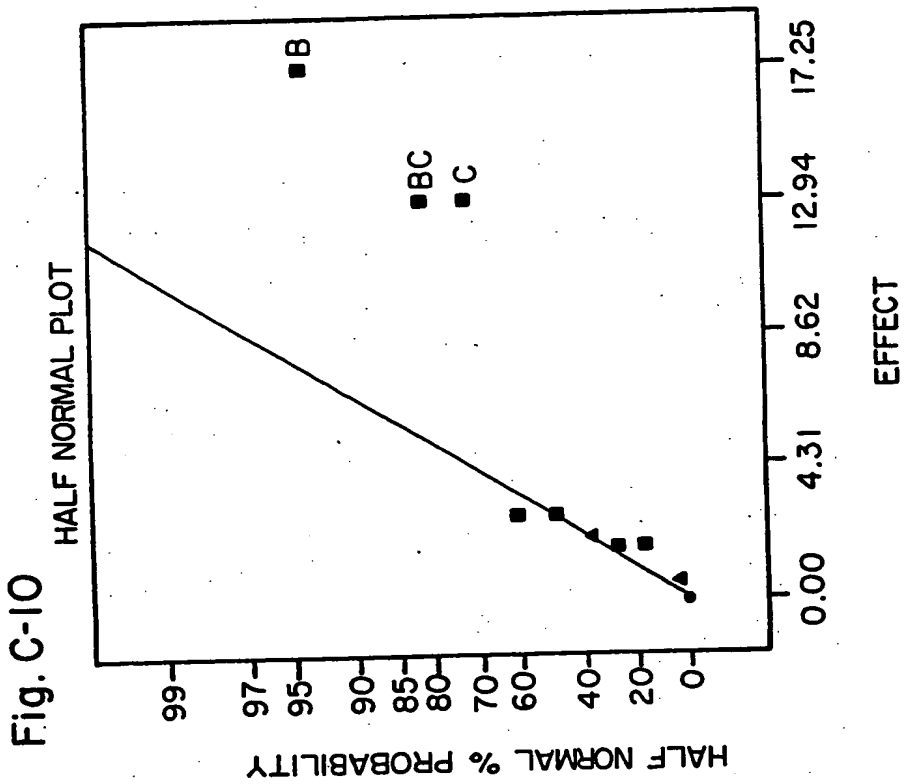
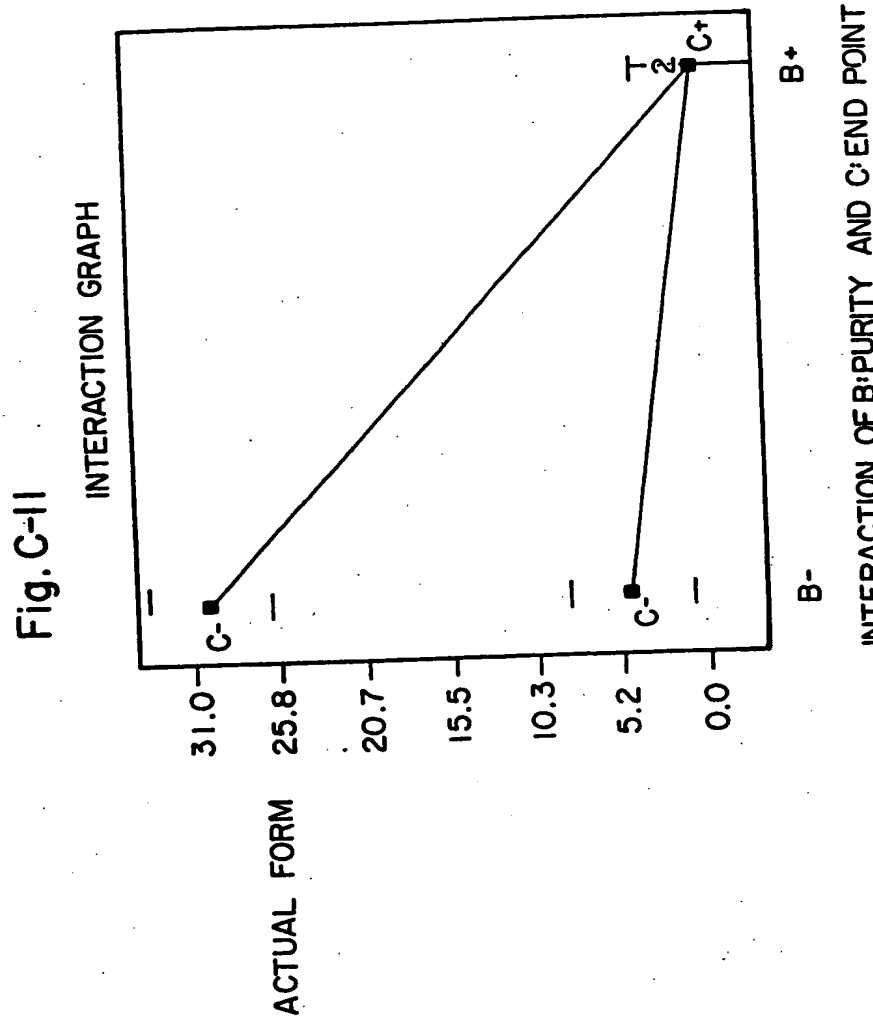


Fig. C-10

FORM

A: COOLING RATE
B: PURITY
C: END POINT

Fig. C-11


INTERACTION GRAPH
ACTUAL FORM
31.0
25.8
20.7
15.5
10.3
5.2
0.0
C-
C+
T2
B-
B+
INTERACTION OF B:PURITY AND C:END POINT

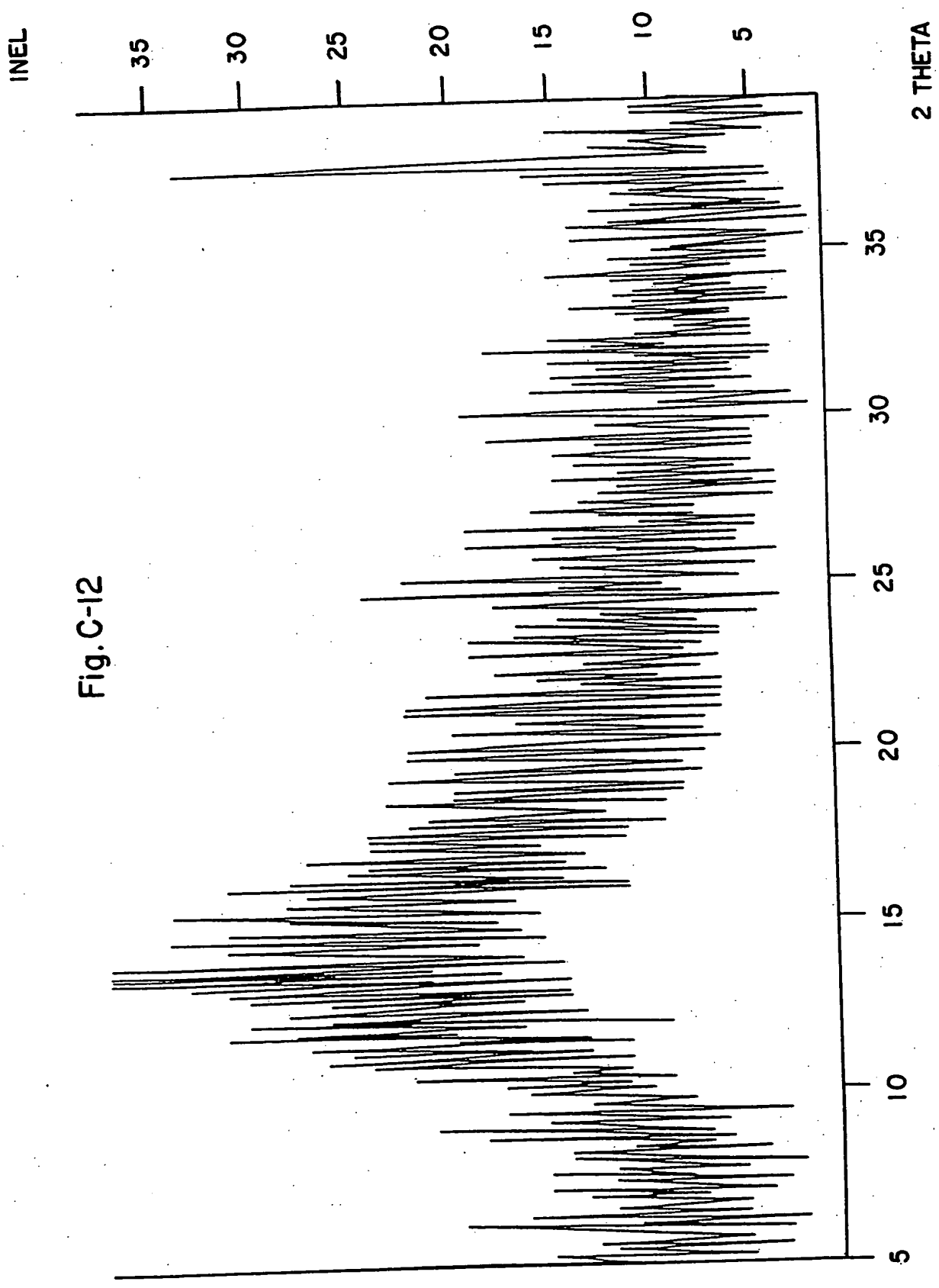


Fig.C-12

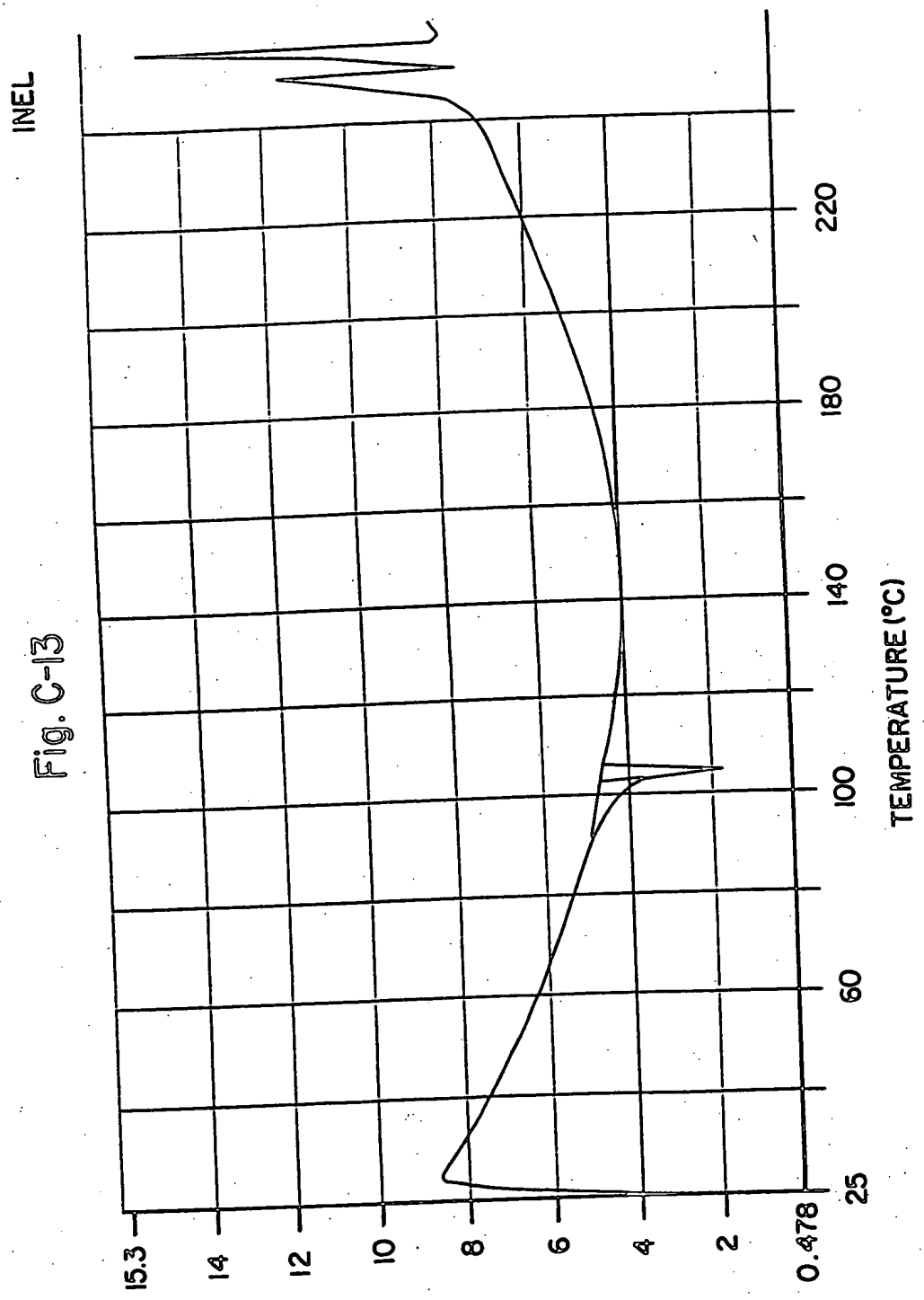
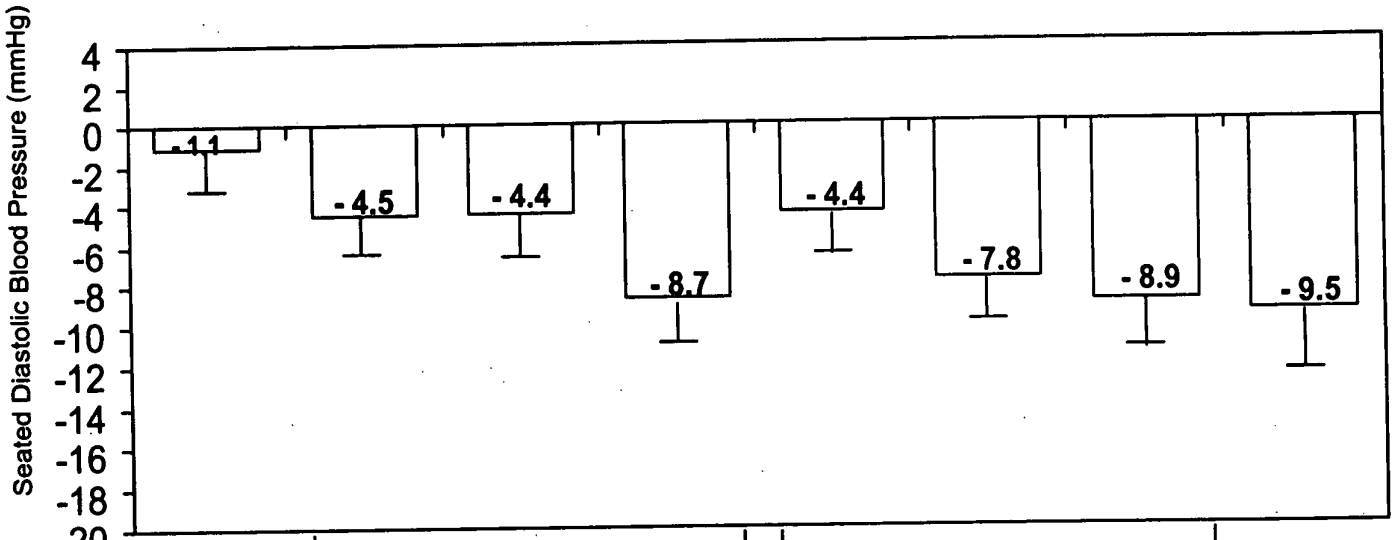


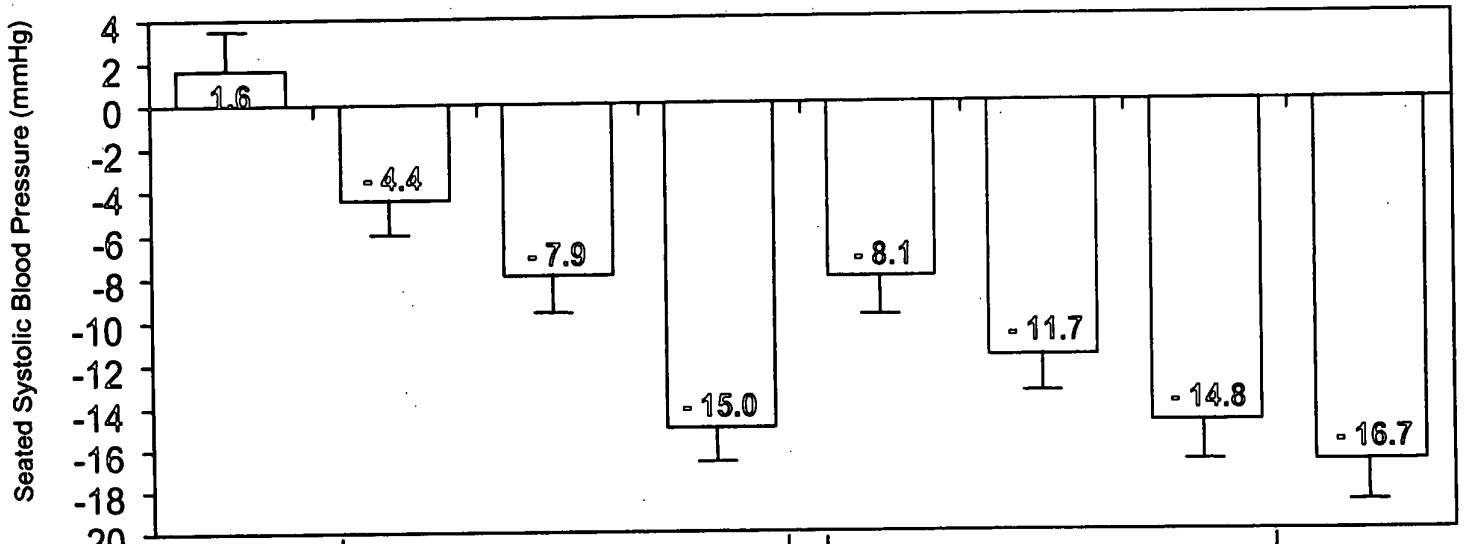
Fig. C-13

Figure D-1 - Mean Change From Baseline in DBP (N = 409)



N	52	54	48	54	53	53	48	47
P-Values vs. Placebo		0.027	0.036	< 0.001	0.031	< 0.001	< 0.001	< 0.001

Figure D-2 - Mean Change From Baseline in SBP (N = 409)



N	52	54	48	54	53	53	48	47
P-Values vs. Placebo		0.022	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

Figure D-3 - Dose Range Factorial Design

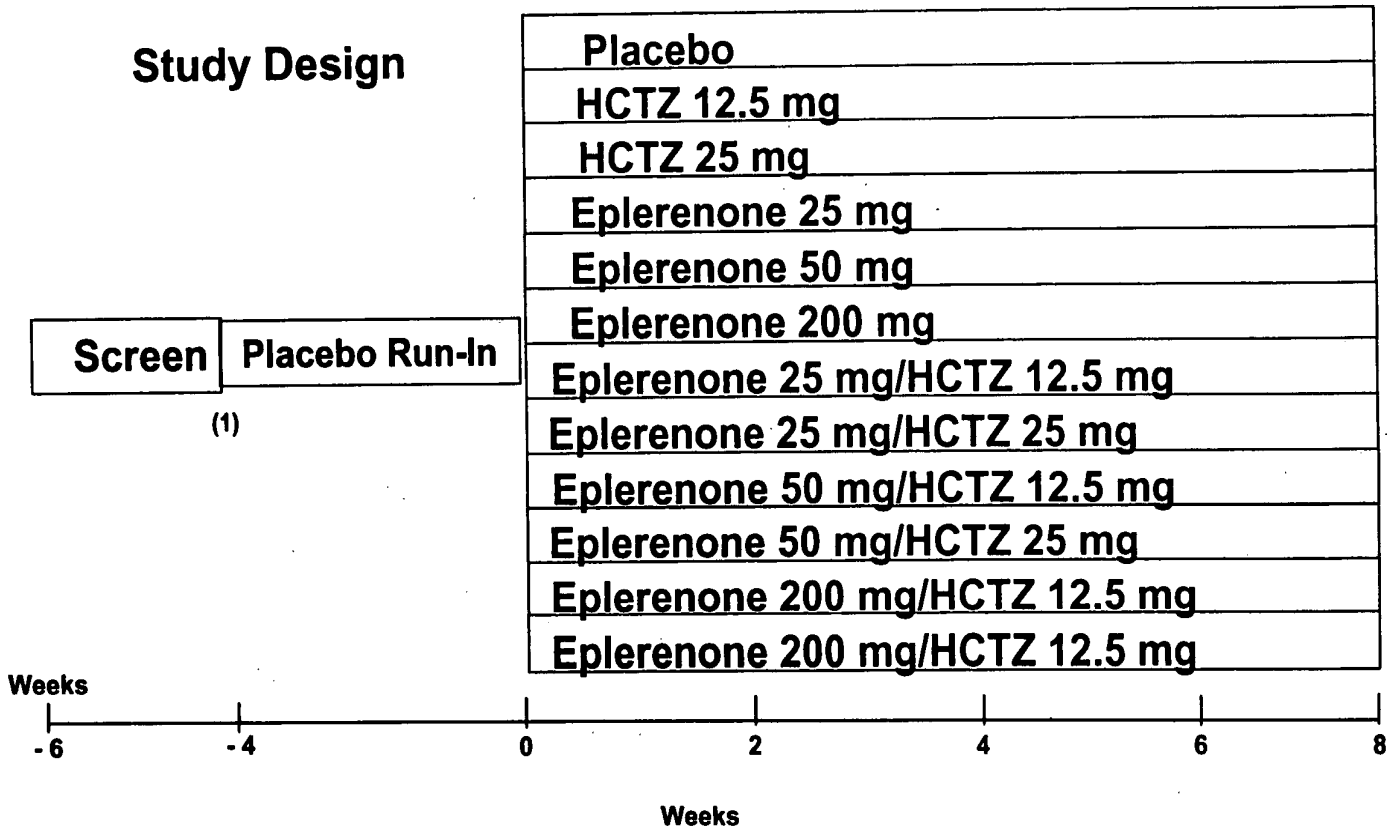
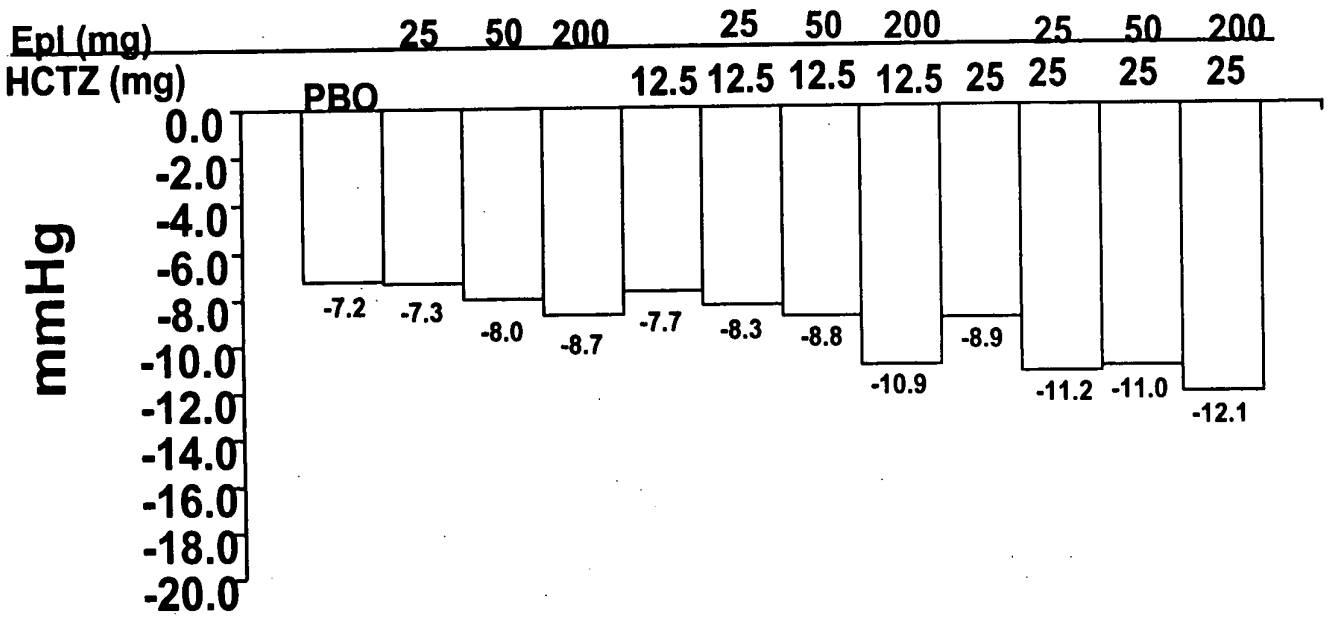


Figure D-4 - Dose-Range Factorial Design - Mean Change in DBP at Final Visit



Figur D-5 - Dose-Range Factorial Design - Mean Change in SBP at Final Visit

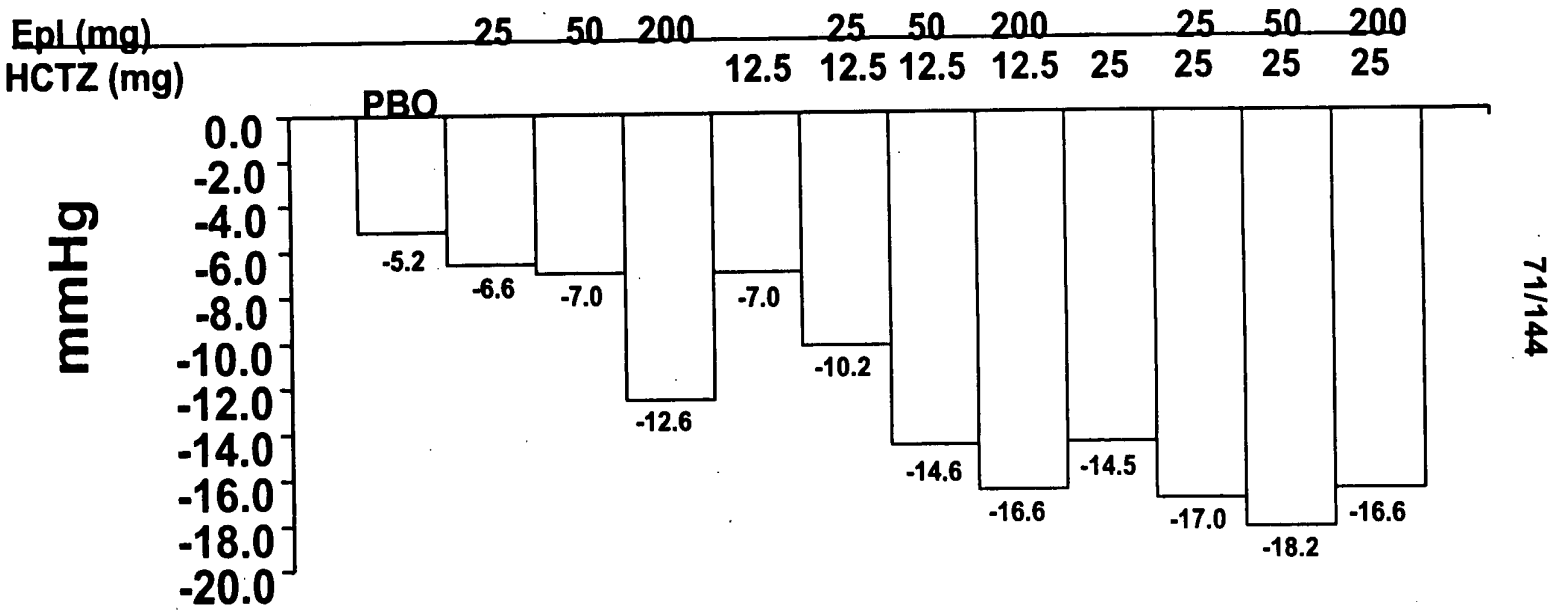
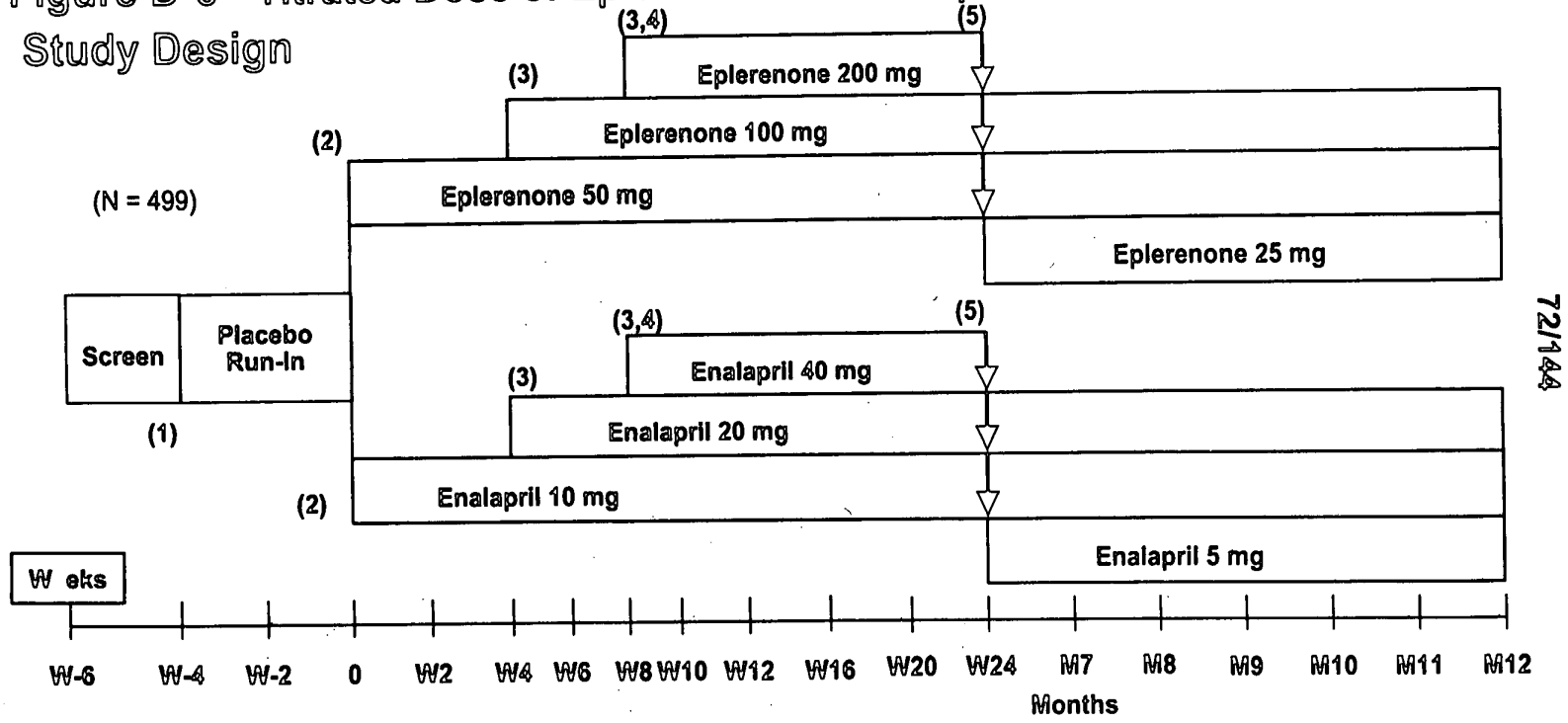


Figure D-6 - Titrated Dose of Eplerenone vs Enalapril Study Design



72/144

Figure D-7 - Titrated Dose of Eplerenone vs Enalapril - Mean Change From Baseline in BP (Week 24)

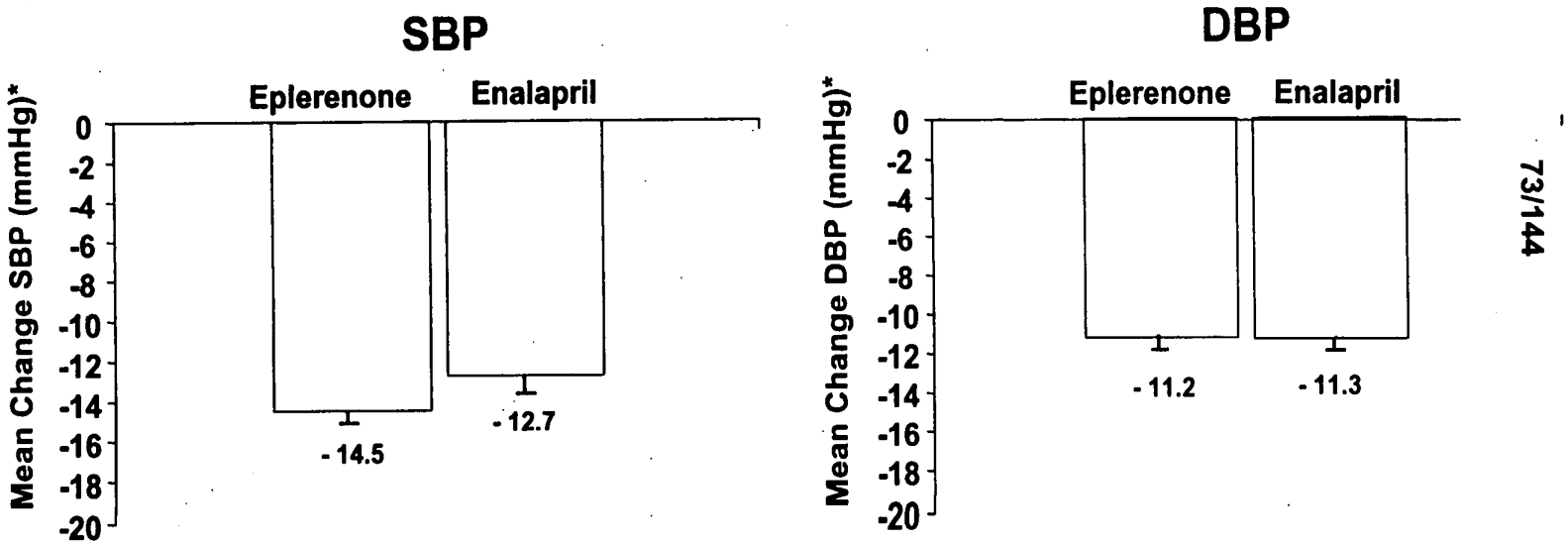


Figure D-8 - Titrated Dose of Eplerenone vs Enalapril

Mean Change From Baseline in BP (Month 12)

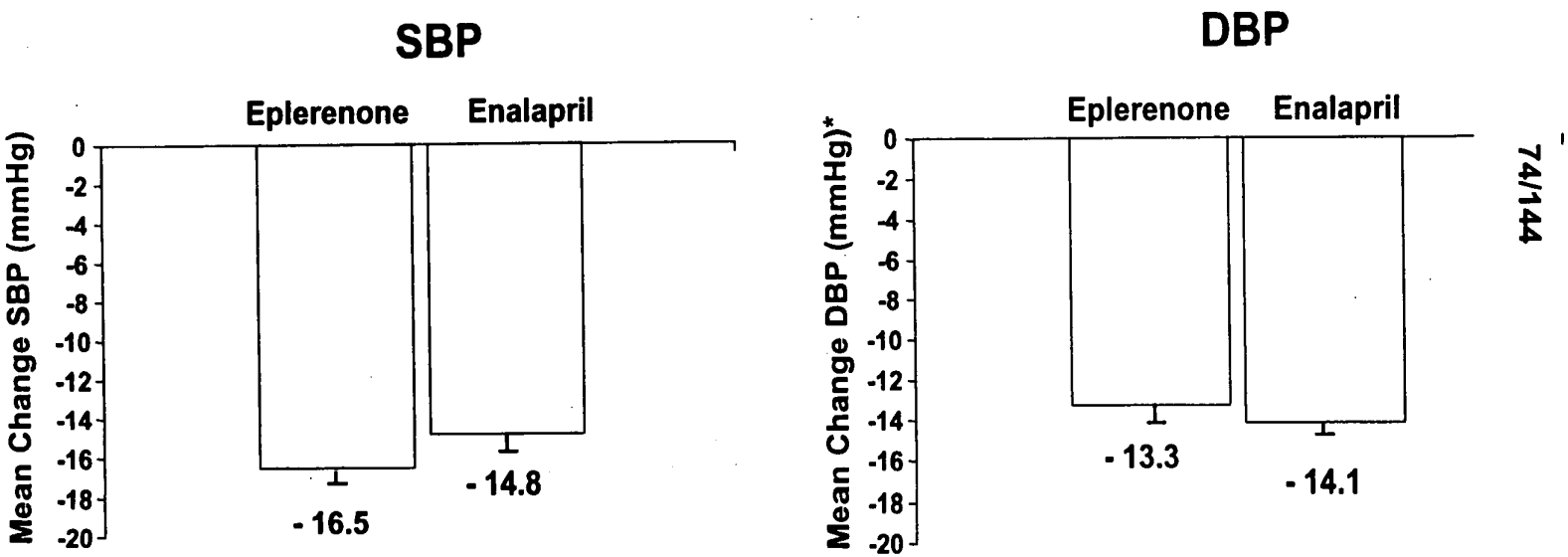


Figure D-9 - Titrated Dose of Eplerenone vs Enalapril
Adverse Events of Special Interest

AEs ([N(%)]	Eplerenone (N = 253)	Enalapril (N = 246)
Hyperkalemia	2 (0.8)	2 (0.8)
Hyperuricemia	2 (0.8)	4 (1.6)
Increased Lab Values		
GGT	3 (1.2)	3 (1.2)
SGOT	2 (0.8)	3 (1.2)
SGPT	3 (1.2)	1 (0.4)
BUN	1 (0.4)	1 (0.4)
Impotence*	1 (0.7)	2 (1.6)
Gynecomastia	2 (0.8)	0
Hypotension	3 (1.2)	1 (0.4)
Hypokalemia	0	0
Menstrual Abnormalities**	0	0

* N = 150 (Eplerenone) and 126 (Enalapril) Male ** N = 103 (Eplerenone) and 120 (Enalapril) Female

Figure D-10 - Eplerenone vs. Enalapril vs. Combination with (LVH) - Study Design

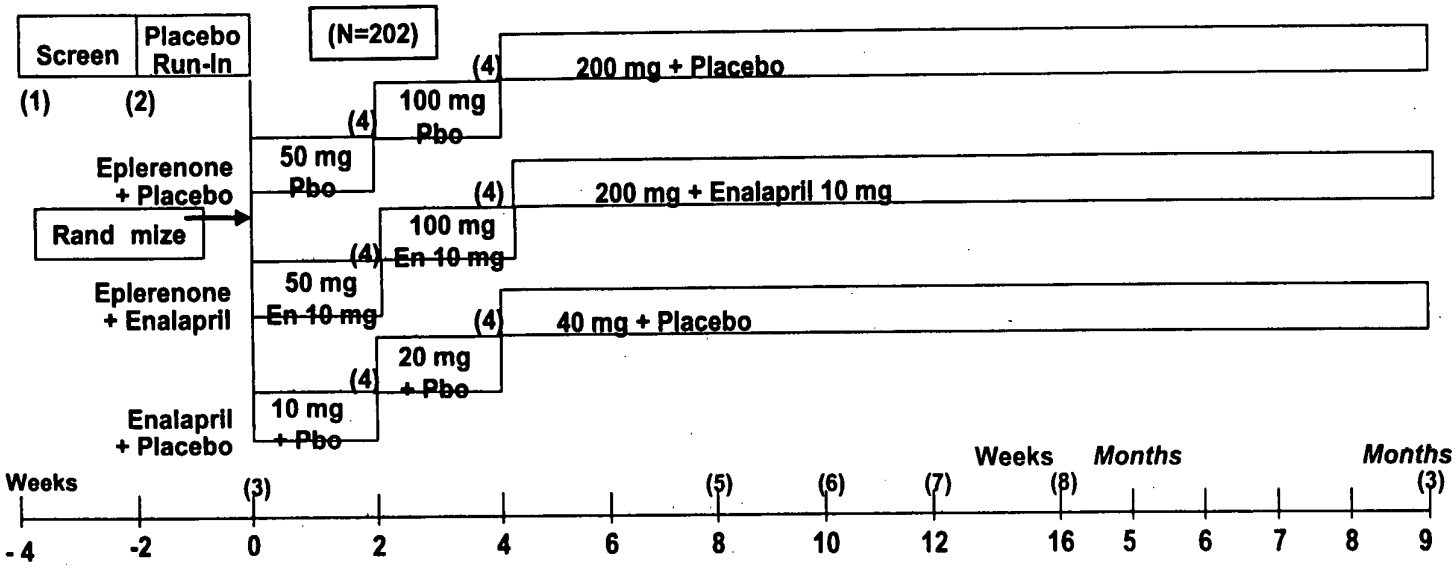
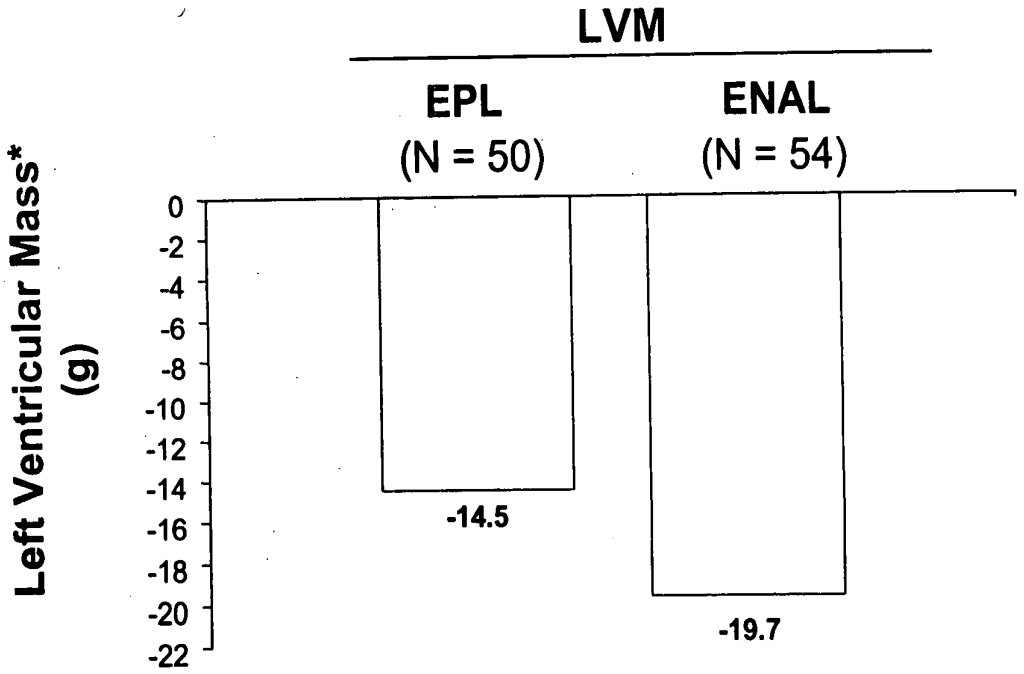


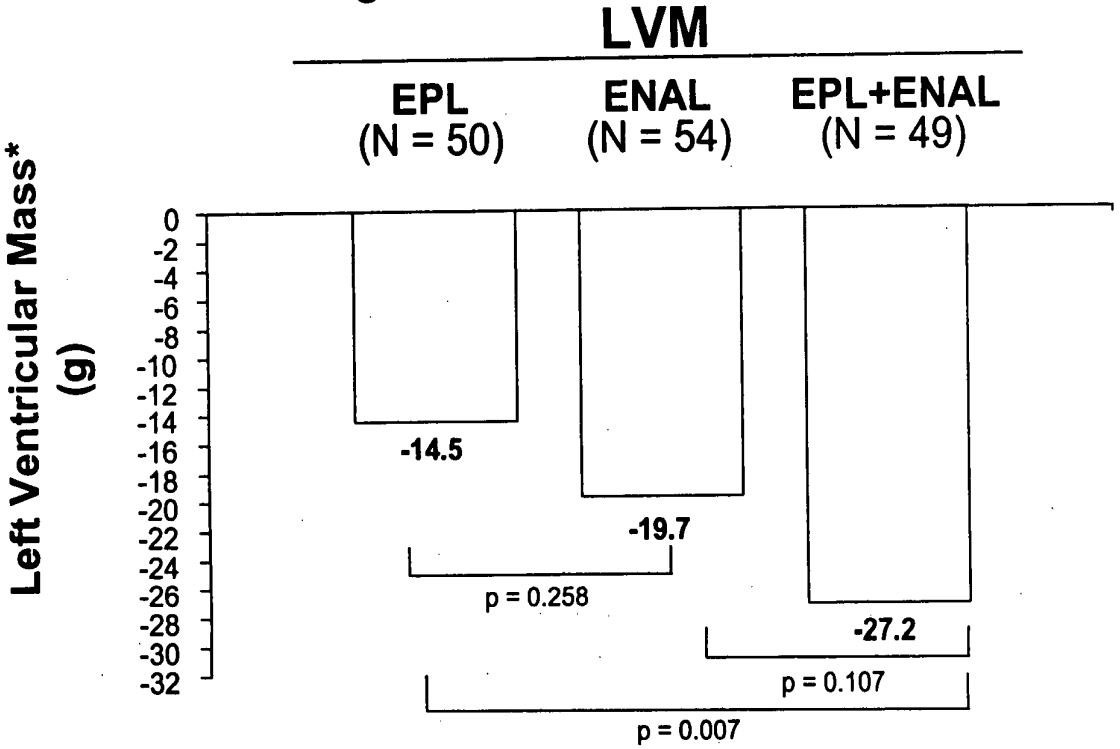
Figure D-11 - Eplerenone vs. Enalapril vs. Combination with (LVH)
Mean Change from Baseline LVM:
Final Visit



Non-inferiority is established if the lower confidence limit for LVM > -15 g
* Adjusted to treatment, center, and baseline value

Figure D-12 - Eplerenone vs. Enalapril vs. Combination with (LVH)

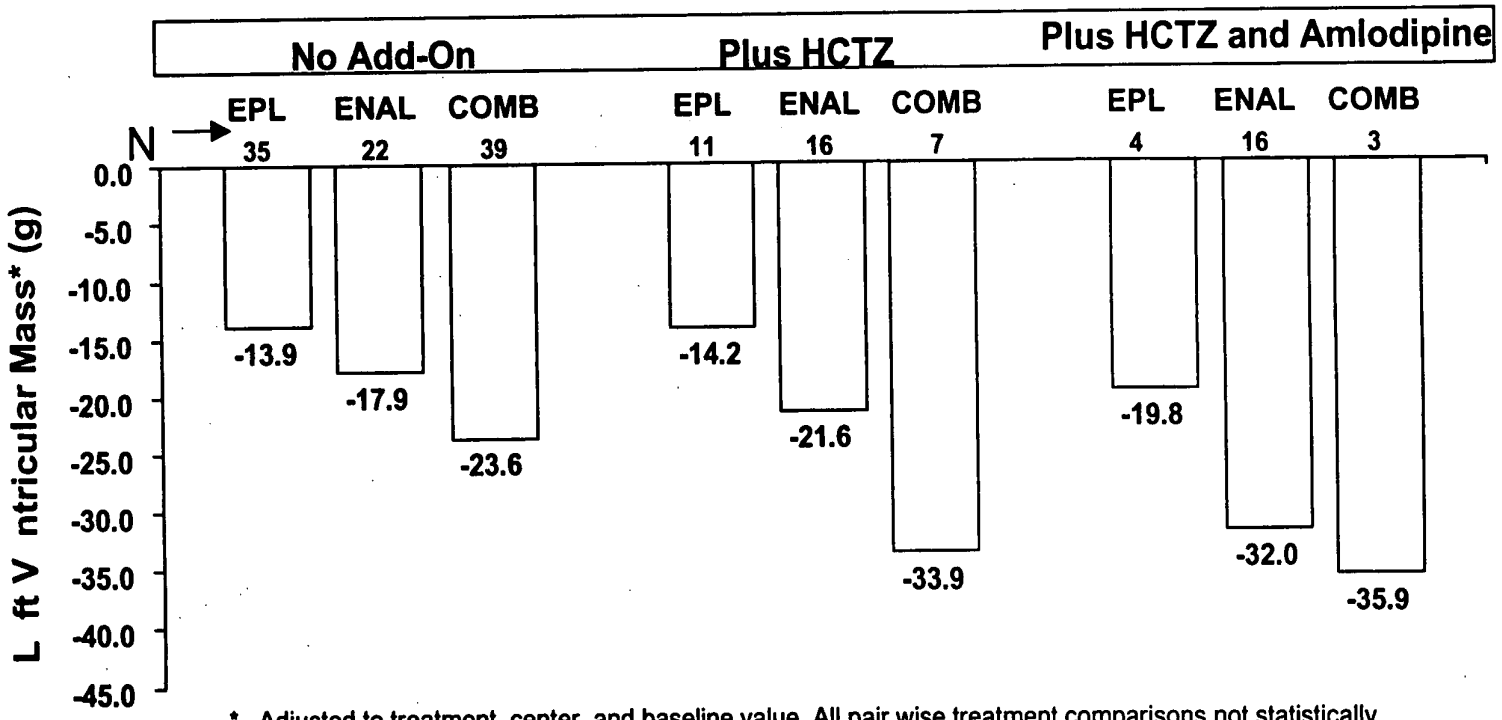
Mean Change from Baseline LVM: Final Visit



* Adjusted to treatment, center, and baseline value. All reductions statistically significant vs. Baseline

Figure D-13 - Eplerenone vs. Enalapril vs. Combination with (LVH)

Mean Change from Baseline in LVM



* Adjusted to treatment, center, and baseline value. All pair wise treatment comparisons not statistically significant

Figure D-14 - Eplerenone vs. Enalapril vs. Combination with (LVH)

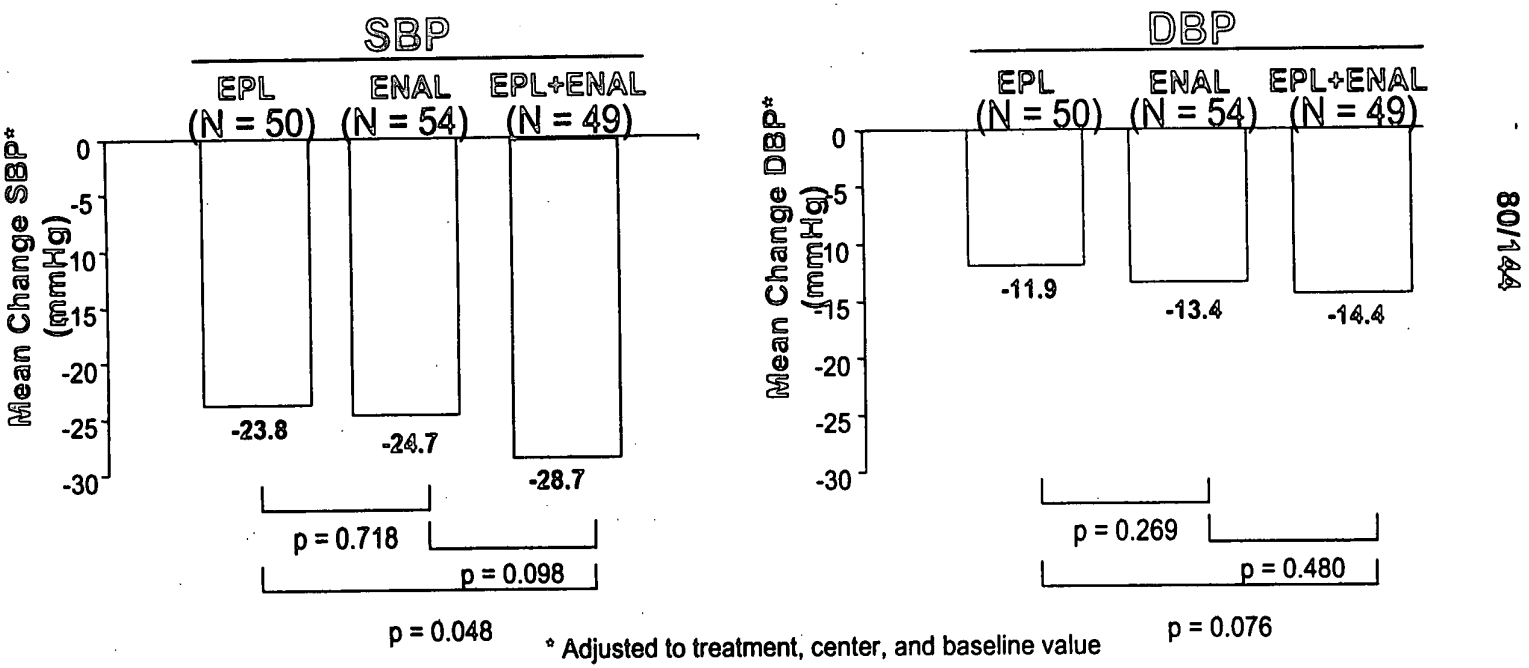


Figure D-15 - Eplerenone vs. Enalapril vs. Combination with (LVH)

Events of Special Interest

AEs [N(%)]	EPL (N = 64)	ENA (N = 71)	EPL+ENA (N = 67)
Hyperkalemia	4 (6.3)	1 (1.4)	1 (1.5)
Hyperuricemia	1 (1.6)	2 (2.8)	0 (0.0)
Increased Lab Values			
GGT	1 (1.6)	3 (4.2)	1 (1.5)
SGOT	2 (3.1)	2 (2.8)	2 (3.0)
SGPT	2 (3.1)	2 (2.8)	0 (0.0)
BUN	1 (1.6)	0 (0.0)	0 (0.0)
Impotence*	0 (0.0)	3 (6.8)	1 (2.2)
Gynecomastia*	1 (2.5)	0 (0.0)	1 (2.2)
Hypotension	1 (1.6)	2 (2.8)	3 (4.5)
Hypokalemia	0 (0.0)	2 (2.8)	0 (0.0)
M nstrual Abnormalities	0 (0.0)	0 (0.0)	0 (0.0)
Br ast Pain, Female	0 (0.0)	0 (0.0)	0 (0.0)
Cough	2 (3.1)	10 (14.1)	6 (9.0)

* N = 40 (EPL); 44 (ENAL); 45 (EPL+ENAL)

Figure D-16 - Low Renin Hypertension Study Design

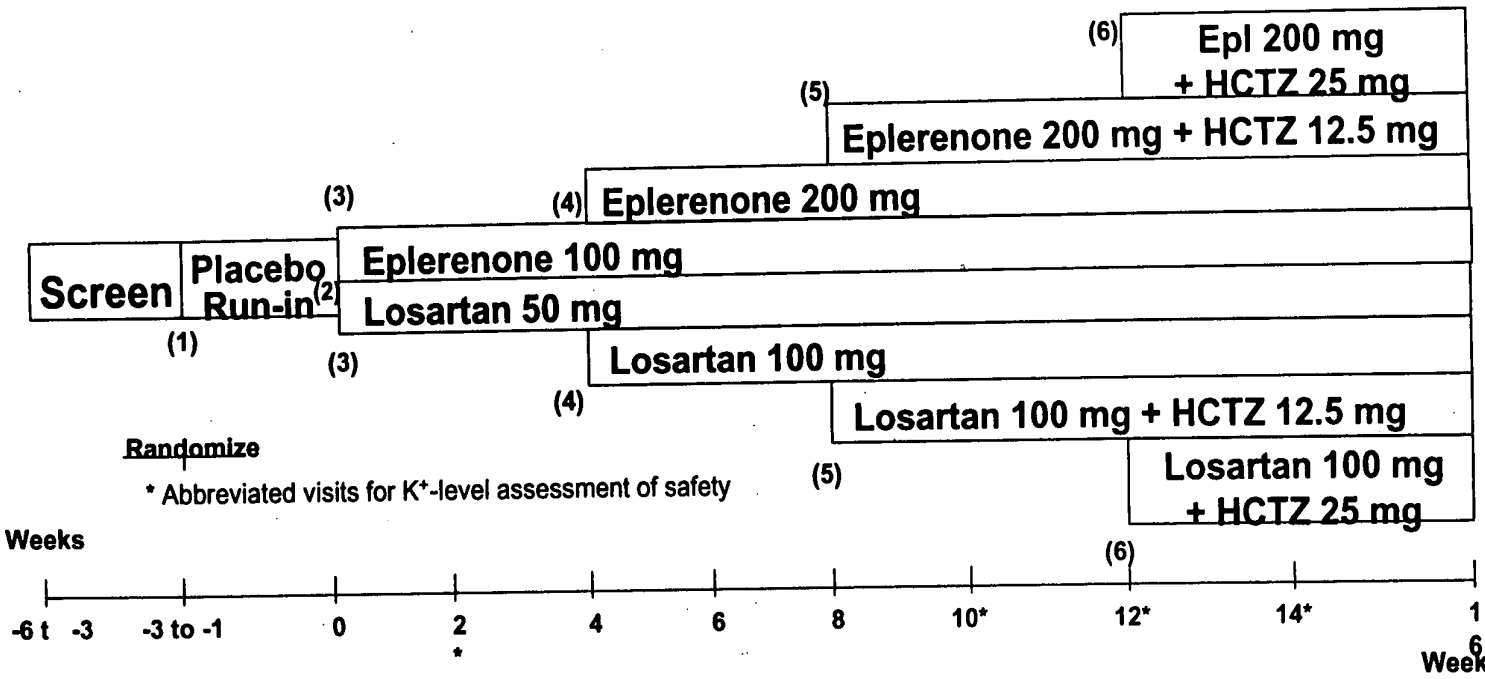
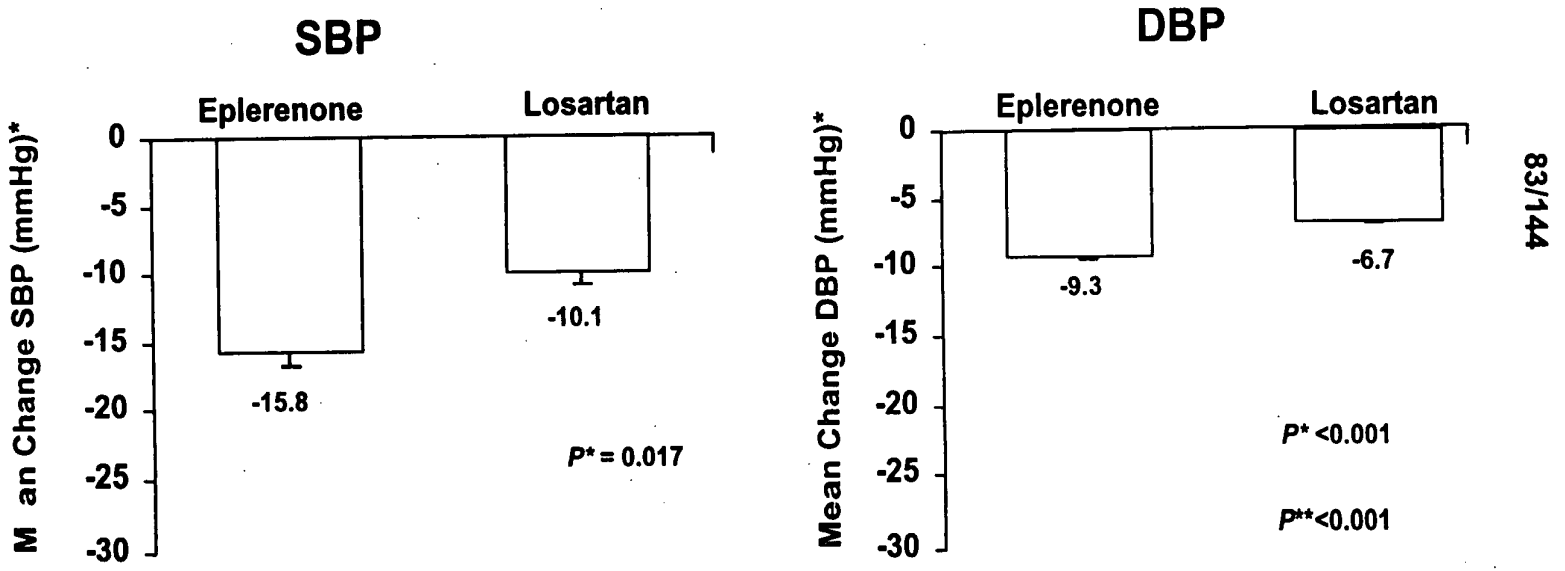


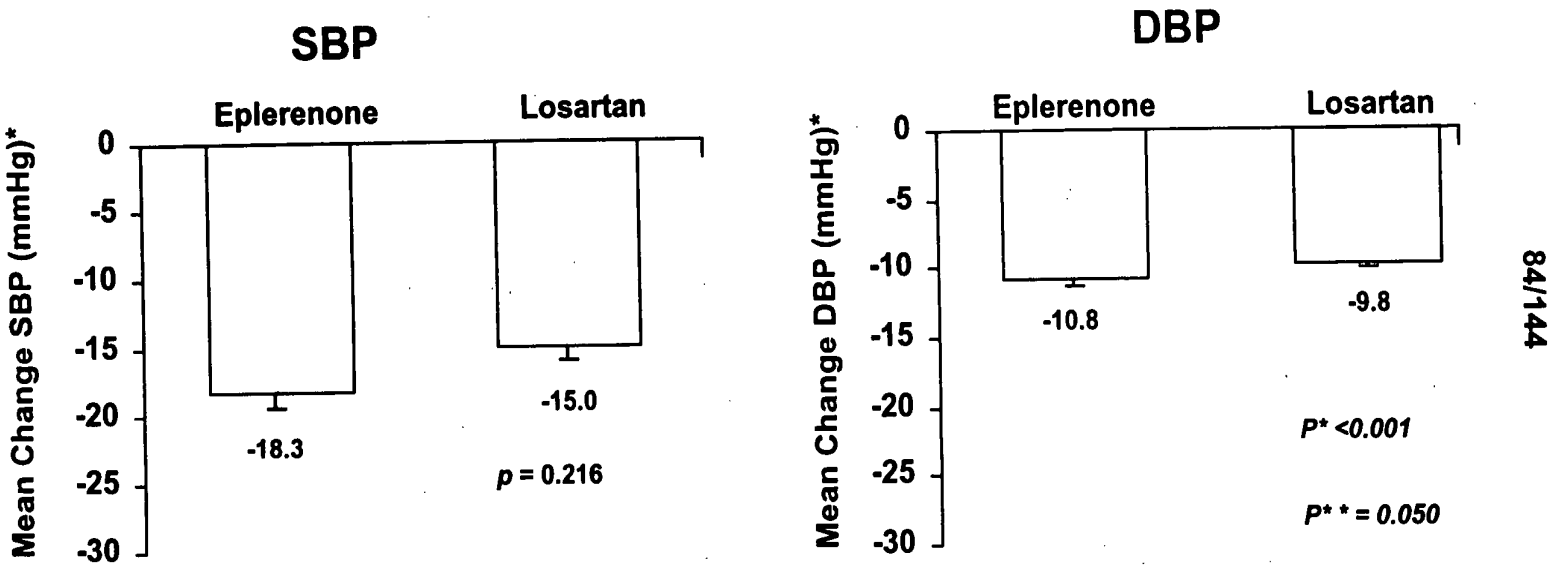
Figure D-17 - Low Renin Hypertension
Mean Change From Baseline in BP
Week 8 (Monotherapy Endpoint)



* Non-Inferiority test ** Two sided test

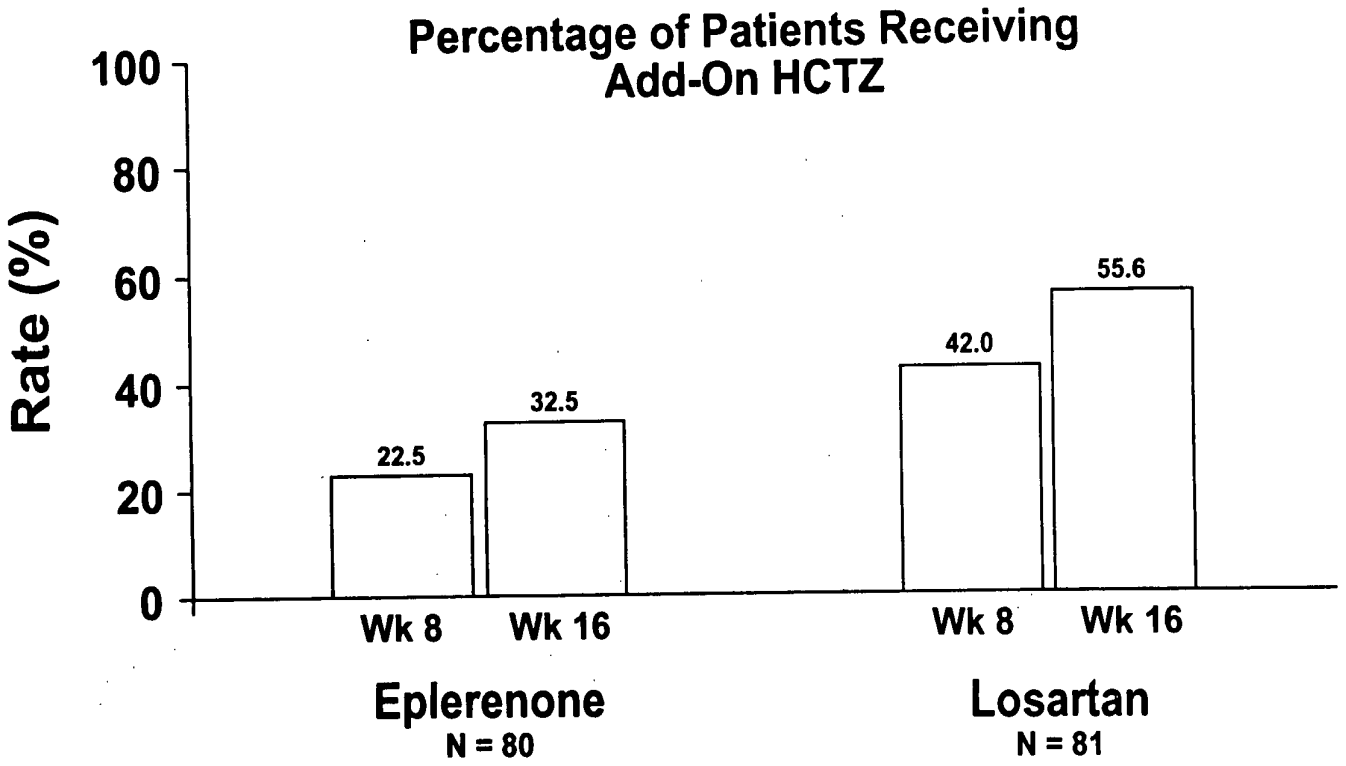
Figure D-18 - Low Renin Hypertension

Mean Change From Baseline in BP
Week 16 (Final Visit)



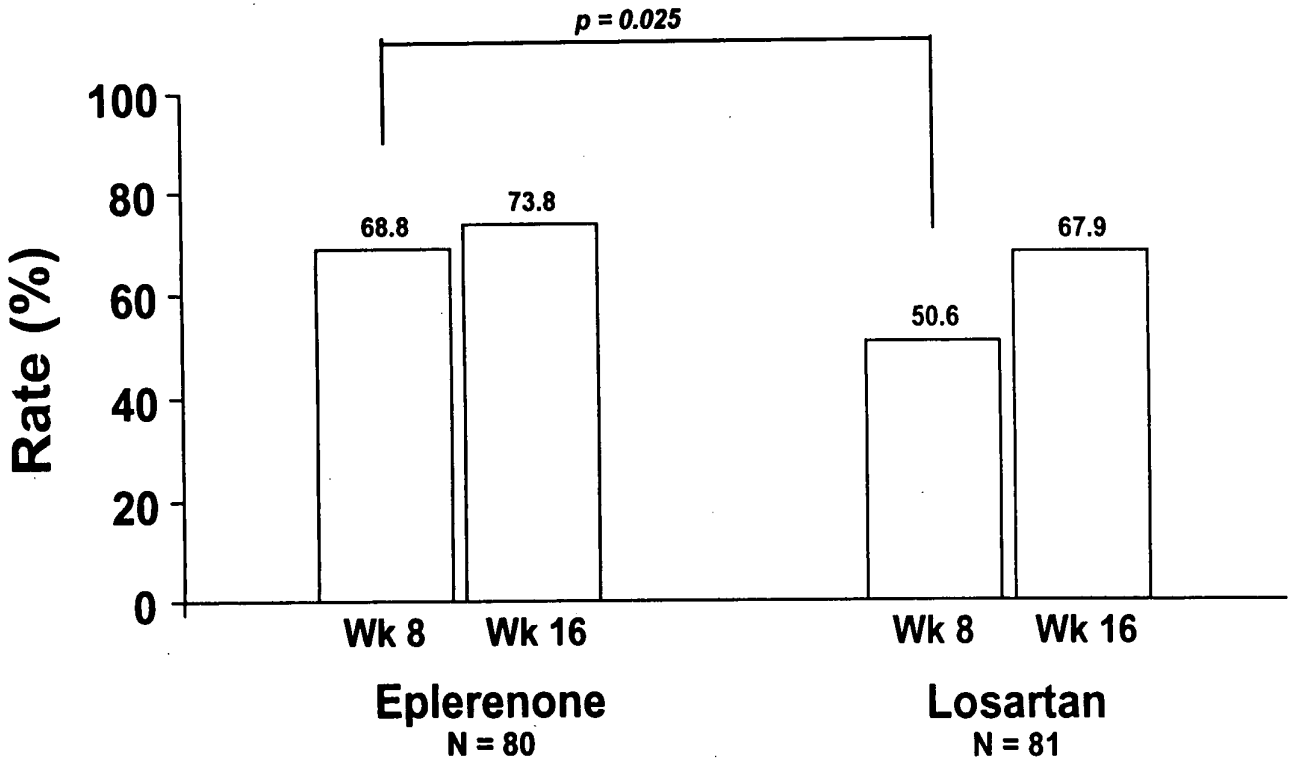
* N n-Inferiority test ** Two sided test

Figure D-19 - Low Renin Hypertension



L g-rank test: $p = 0.002$

Figure D-20 - Low Renin Hypertension - Responder Rates



Responder defined as: seDBP < 90 mmHg or seDBP ≥10 mmHg reduction from baseline

Figure D-21 - Low Renin Hypertension - Adverse Events of Special Interest

Adverse Events N (%)	Eplerenone (N = 86)	Losartan (N = 82)
Gynecomastia*	2 (5.0)	0 (0.0)
Menstrual Disorder	0 (0.0)	1 (2.8)
Hyperkalemia	0 (0.0)	0 (0.0)
Hyperuricemia	2 (2.3)	3 (3.7)
Impotence*	1 (2.5)	1 (2.2)
Increased Lab Values		
GGT	2 (2.3)	1 (1.2)
SGOT	2 (2.3)	1 (1.2)
SGPT	2 (2.3)	1 (1.2)
BUN	0 (0.0)	1 (1.2)
Hypotension	0 (0.0)	0 (0.0)

* Eplerenone N = 40; Losartan N = 46

Figure D-22 - Comparison in Black and White Populations

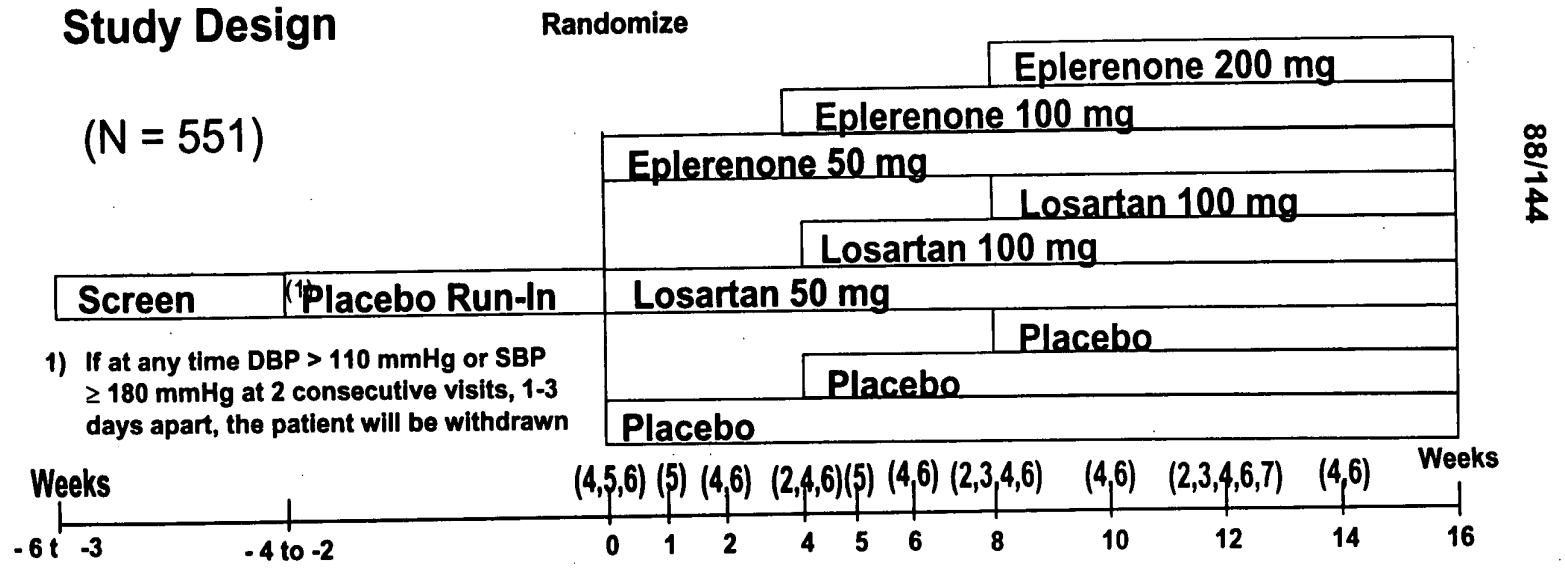
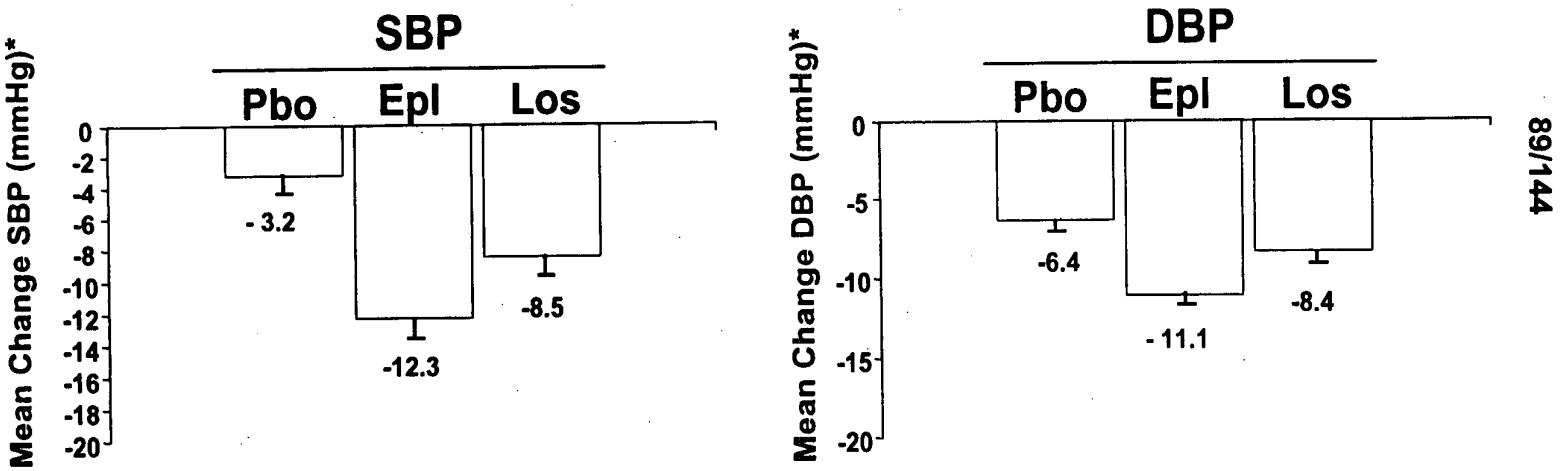


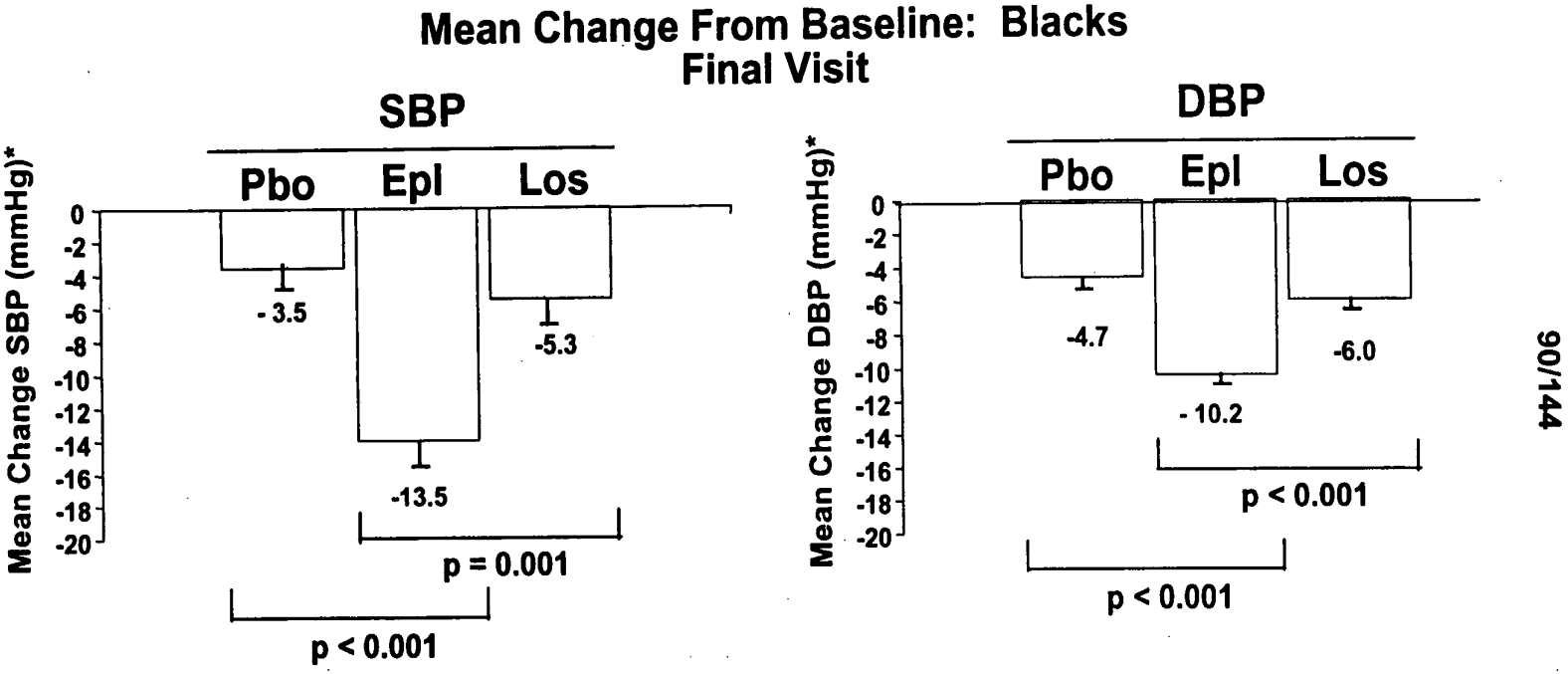
Figure D-23 - Comparison in Black and White Populations

Mean Change From Baseline: Whites
Final Visit



* Adjusted to treatment, center, and baseline value

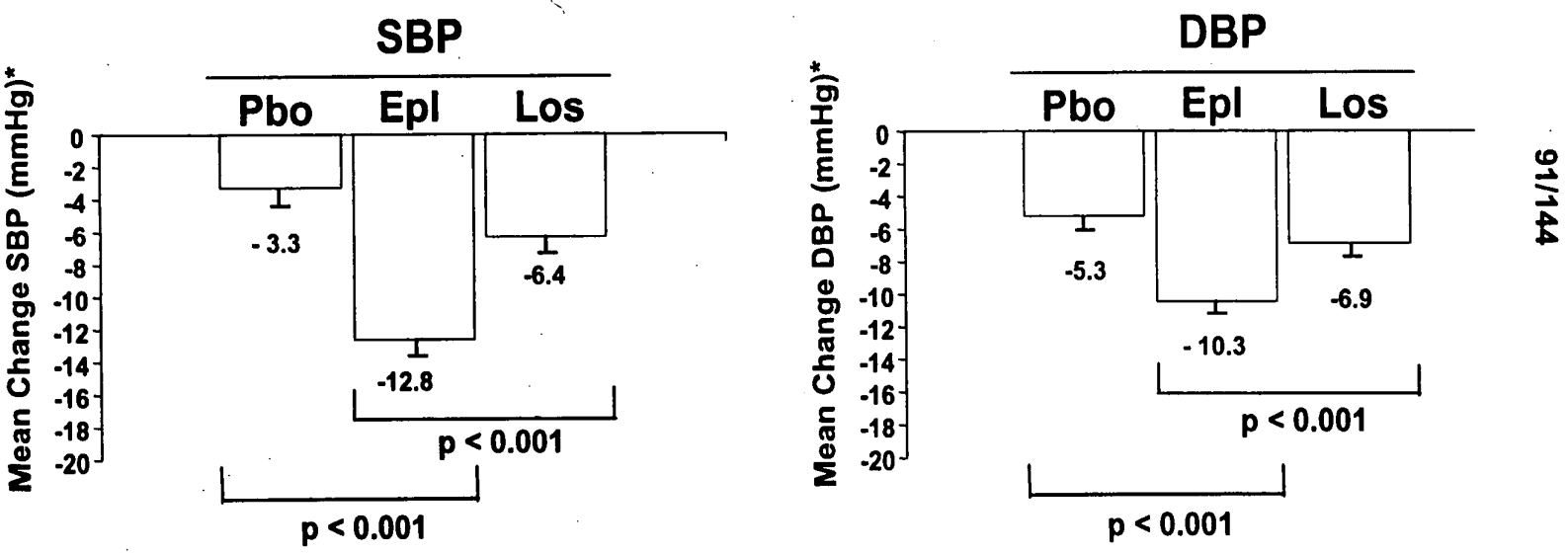
Figure D-24 - Comparison in Black and White Populations



* Adjusted to treatment, center, and baseline value

Figure D-25 - Comparison in Black and White Populations

Mean Change From Baseline: All Patients Final Visit



* Adjusted to treatment, center, and baseline value

Figure D-26 - Comparison in Black and White Populations Adverse Events of Special Interest

	All Patients		
AEs ([N(%)]	Pbo (N = 181)	Epl (N = 182)	Los (N = 188)
Hyperkalemia	1 (0.6)	1 (0.5)	0
Hyperuricemia	0	0	0
Increased Lab Values			
GGT	0	0	2 (1.1)
SGOT	1 (0.6)	0	1 (0.5)
SGPT	2 (1.1)	0	1 (0.5)
BUN	0	0	0
Impotence*	1 (1.2)	0	1 (1.2)
Gyn comastia	0	0	0
Hypotension	0	0	0
Hypokalemia	1 (0.6)	0	1 (0.5)
Menstrual Abnormalities**	0	1 (0.9)	2 (1.1)

N = 84 (Pbo); 65 (Epl); 83 (Los)

**N = 97 (Pbo); 117 (Epl); 105 (Los)

Figure D-27 - Study Design

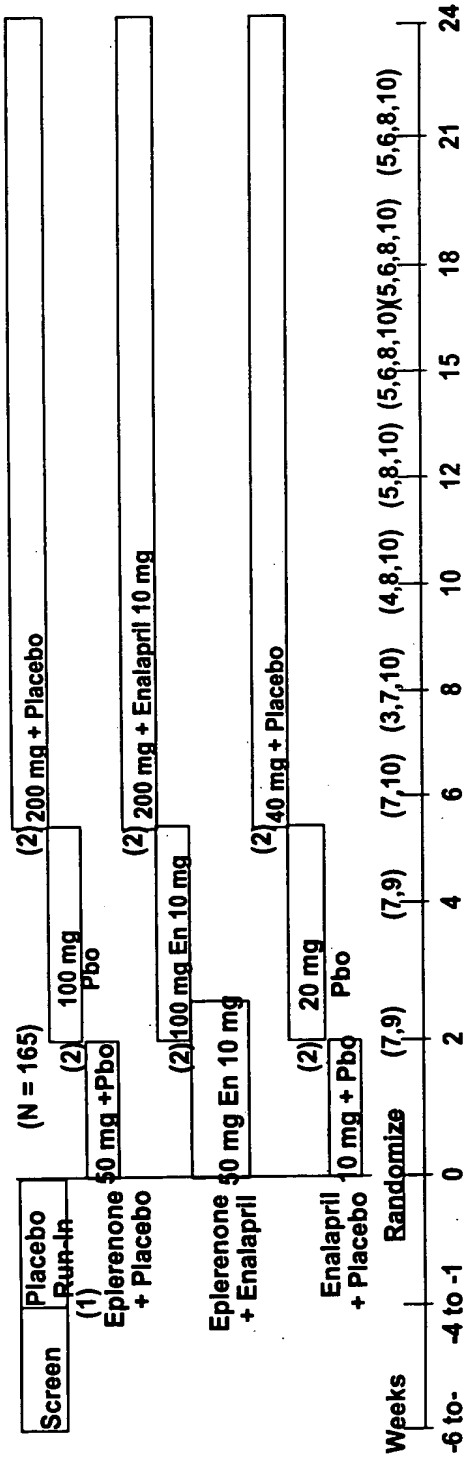
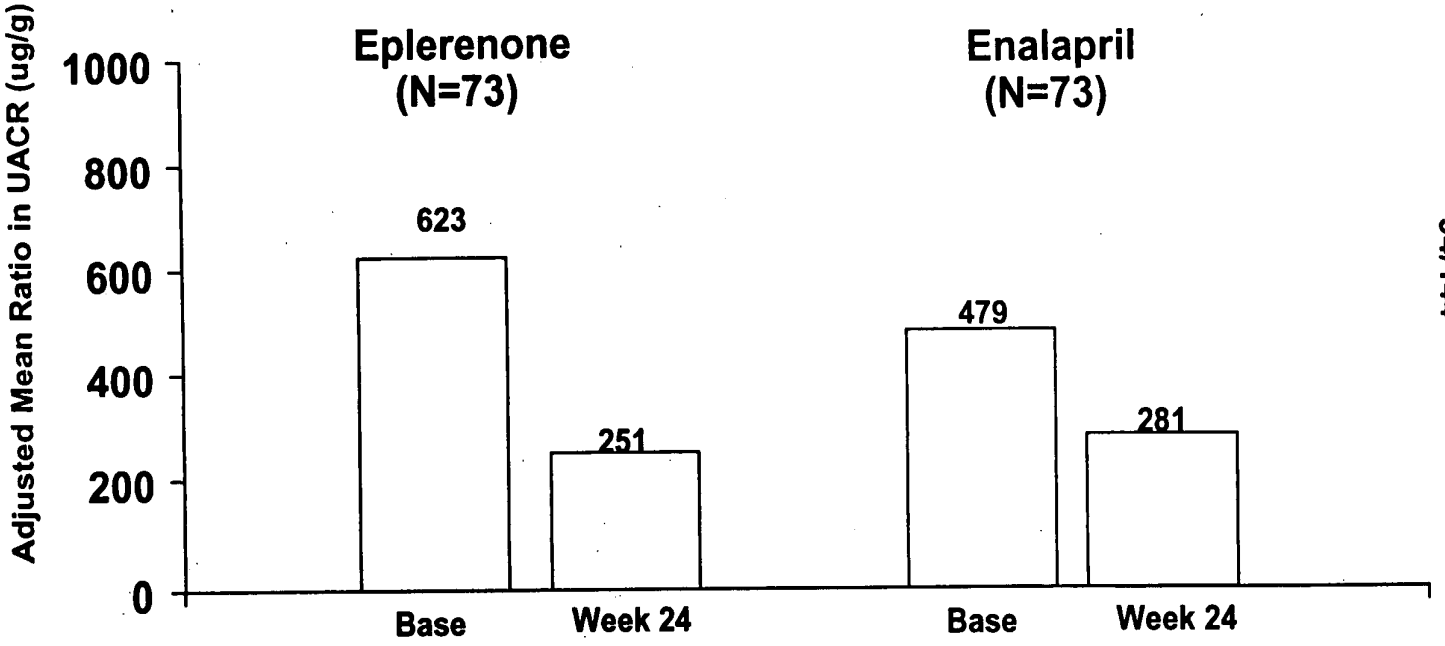


Figure D-28 - Mean Change From Baseline: UACR at Week 24



94/144

* Adjusted for treatment, center, and baseline

Figure D-29 - Geometric Mean of UACR (ug/g) at Week 8 and Week 24

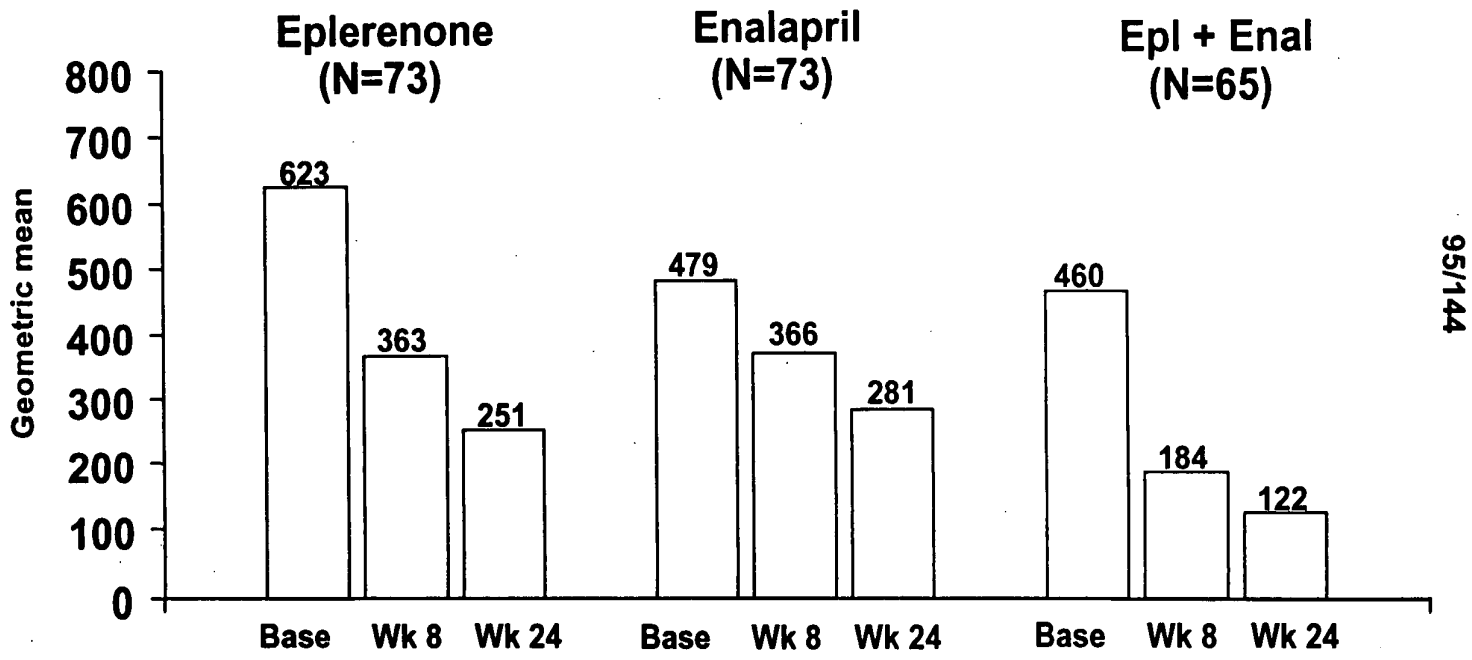


Figure D-30 - Mean Change from Baseline in SBP at Week 8 and Week 24

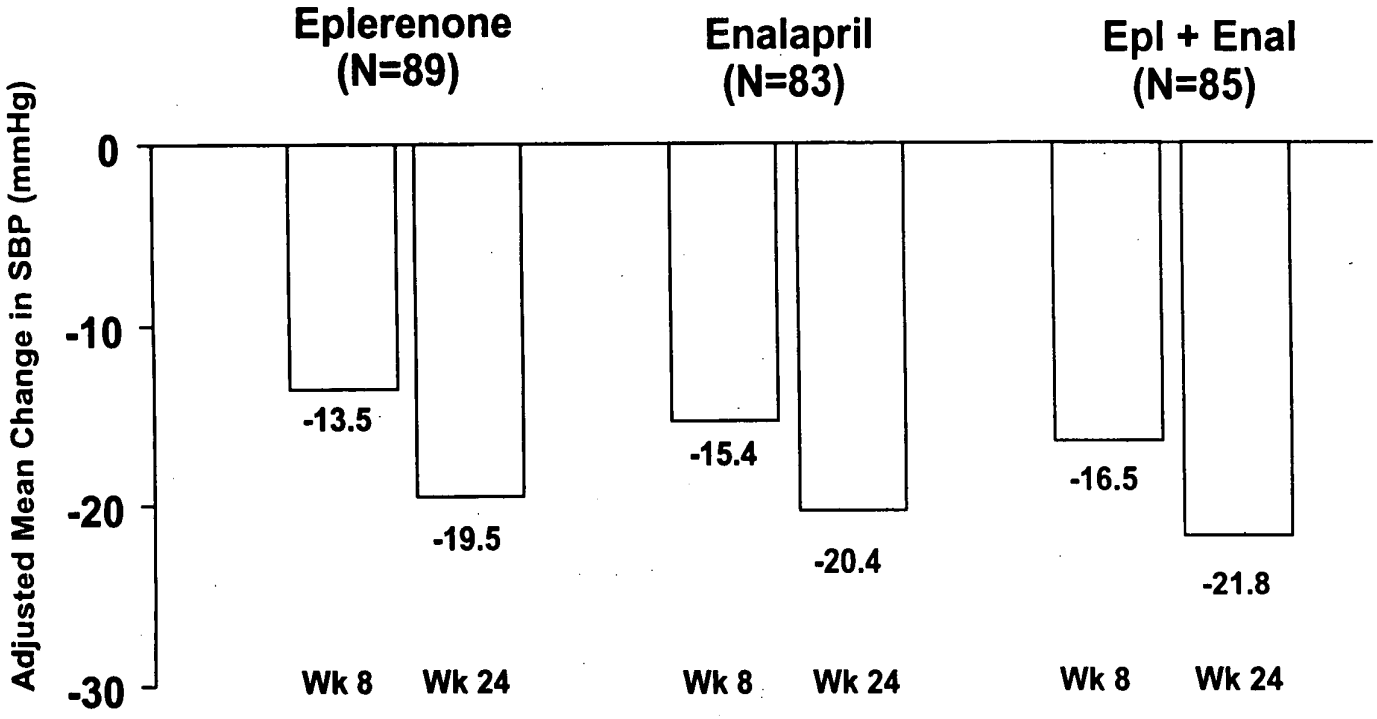
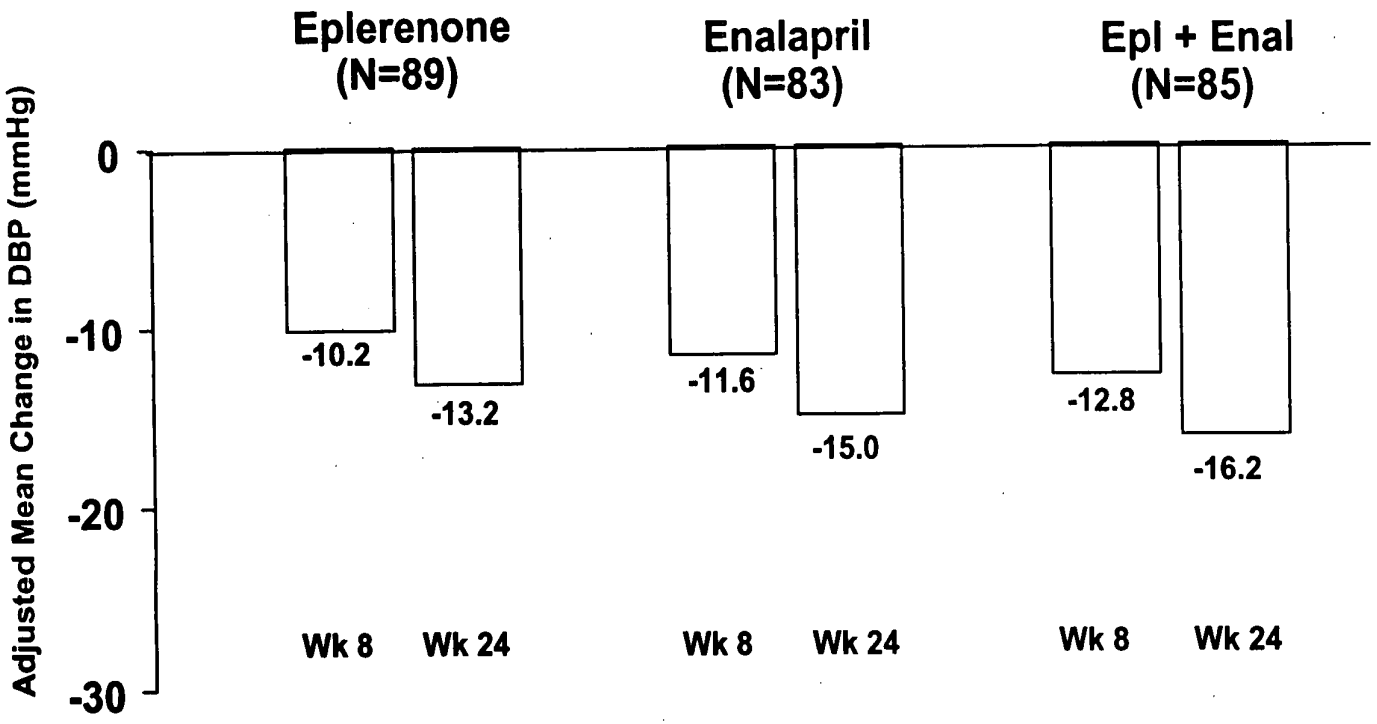


Figure D-31 - **Mean Change from Baseline in DBP at Week 8 and Week 24**



97/144

Figure D-32 - Adverse Events of Special Interest

AEs ([N(%)]	Epl (N = 93)	Enal (N = 84)	Epl + Enal (N = 89)
Hyperkalemia	15 (16.1)	5 (6.0)	21 (24.1)
Hyperuricemia	4 (4.3)	1 (1.2)	0 (0.0)
Increased Lab Values			
GGT	3 (3.2)	3 (3.6)	2 (2.3)
SGOT	2 (2.2)	1 (1.2)	1 (1.1)
SGPT	2 (2.2)	2 (2.4)	1 (1.1)
BUN	5 (5.4)	0 (0.0)	3 (3.4)
Impotence	0 (0.0)	1 (2.0)	0 (0.0)
Gynecomastia	0 (0.0)	0 (0.0)	0 (0.0)
Hypotension	0 (0.0)	0 (0.0)	0 (0.0)
Hypokalemia	0 (0.0)	0 (0.0)	0 (0.0)
Menstrual Abnormalities	1 (2.5)	2 (6.1)	0 (0.0)

Figure D-33 - Eplerenone vs. Amlodipine in Elevated SBP
Study Design

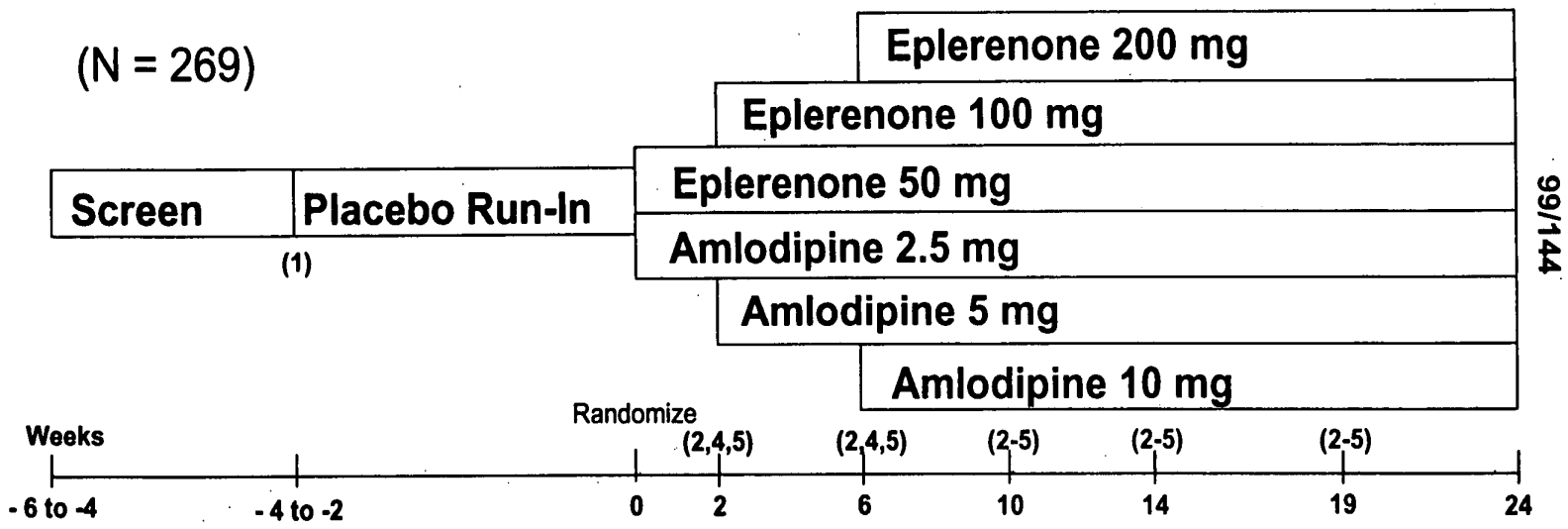


Figure D-34 - Eplerenone vs. Amlodipine in Elevated SBP

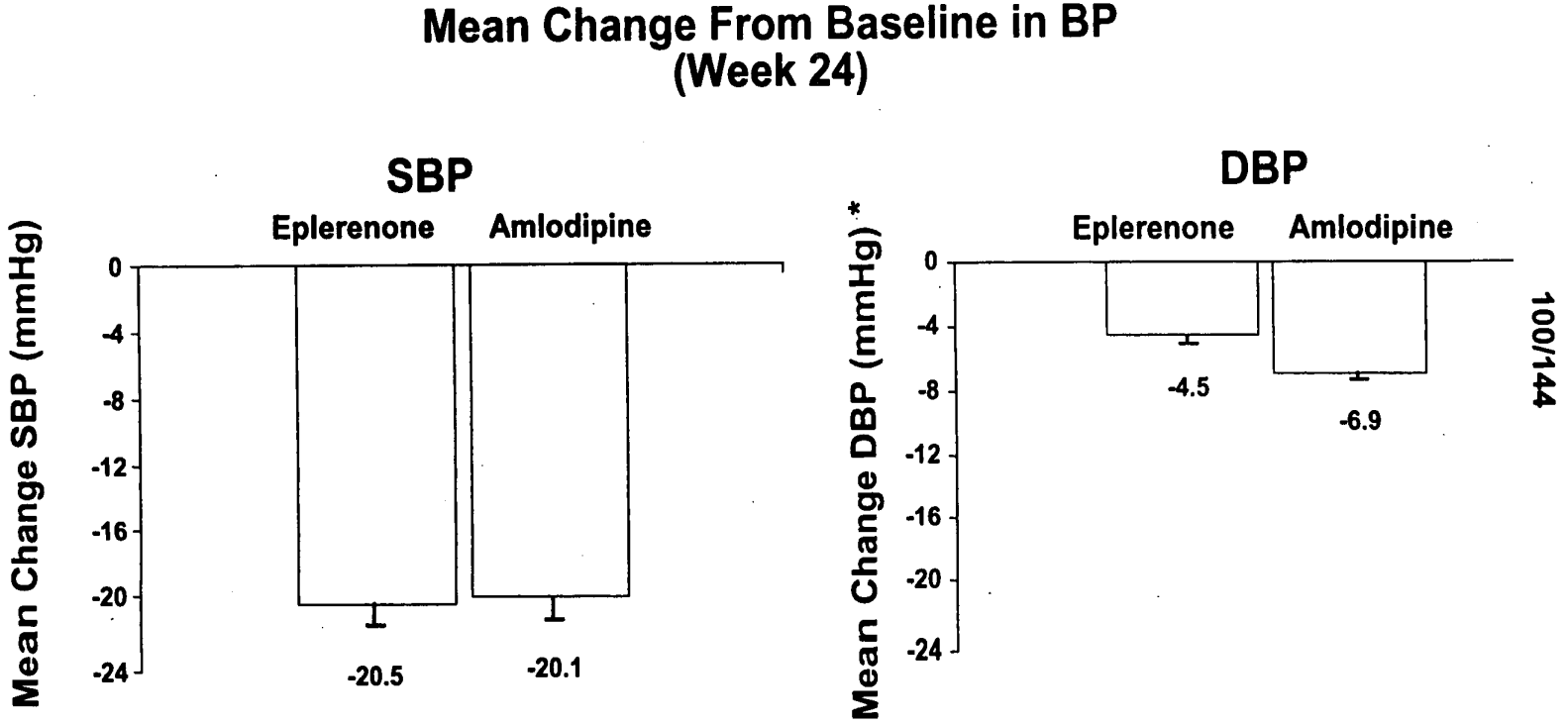
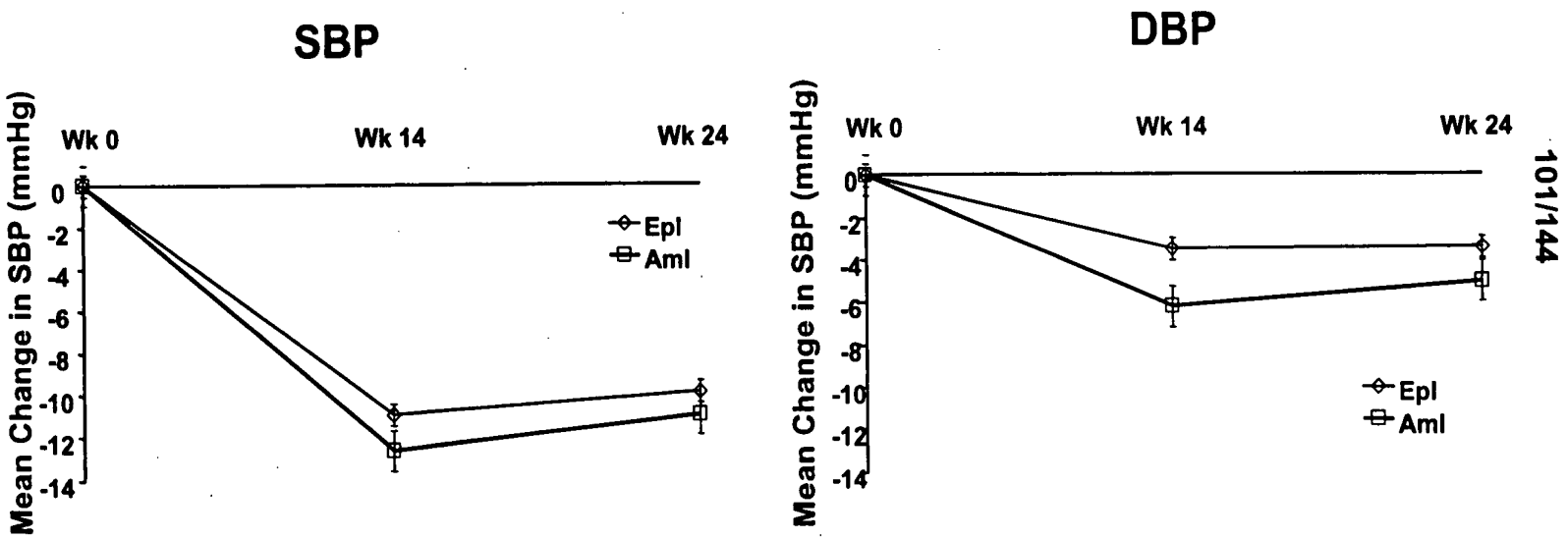


Figure D-35 - Eplerenone vs. Amlodipine in Elevated SBP

Mean Change From Baseline in 24-Hour Mean BP ABPM Measurements



* Adjusted for treatment, center, and baseline value

Figure D-36 - Eplerenone vs. Amlodipine in Elevated SBP
Mean Change From Baseline in 24-Hour Mean PP ABPM Measurements

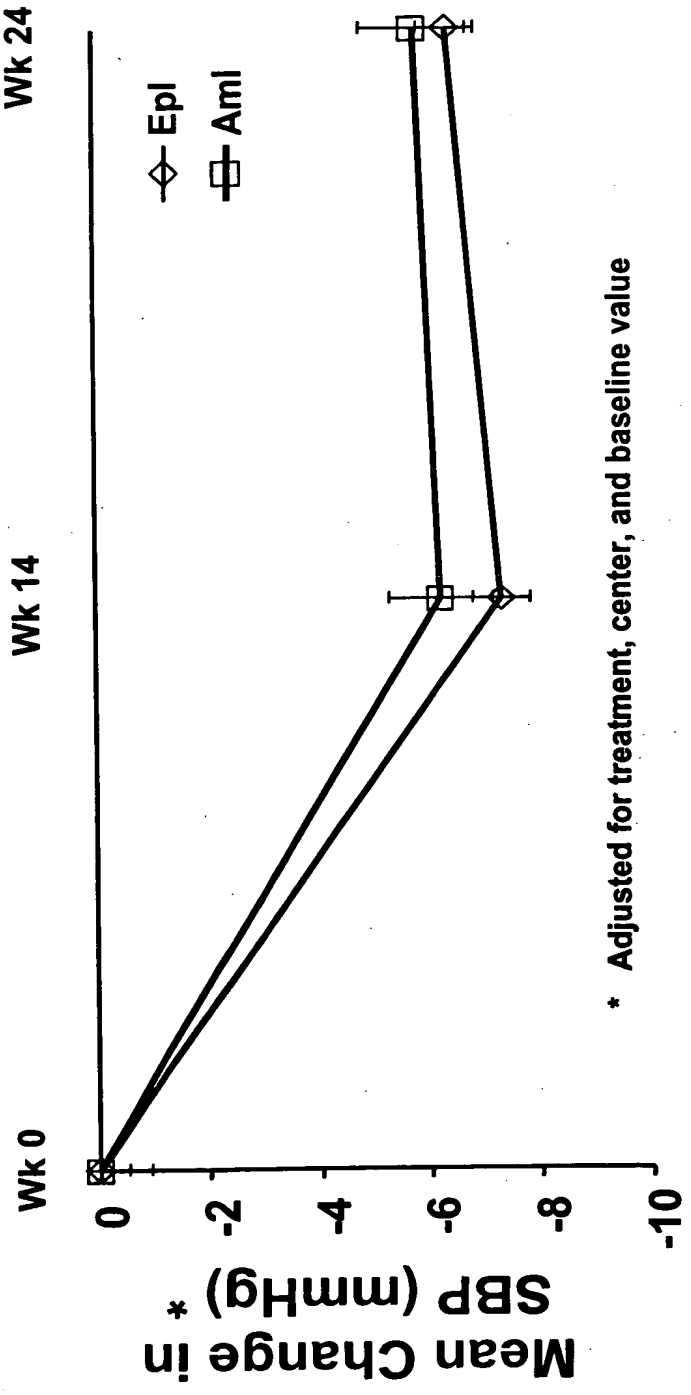
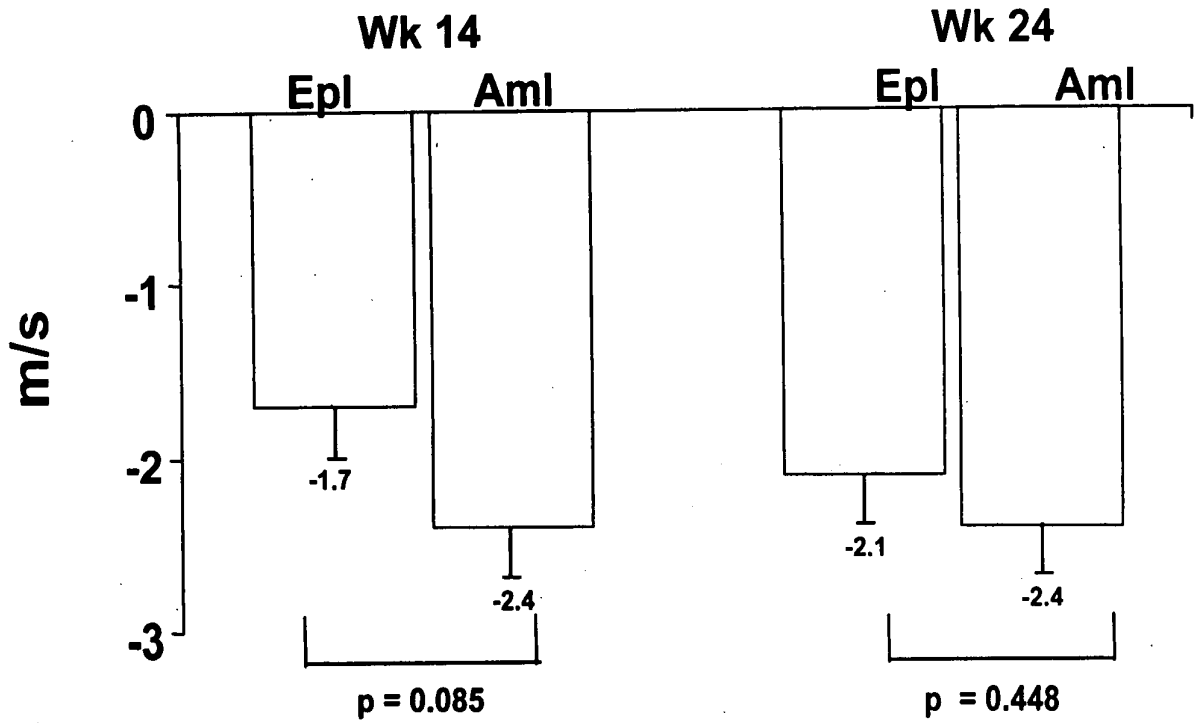
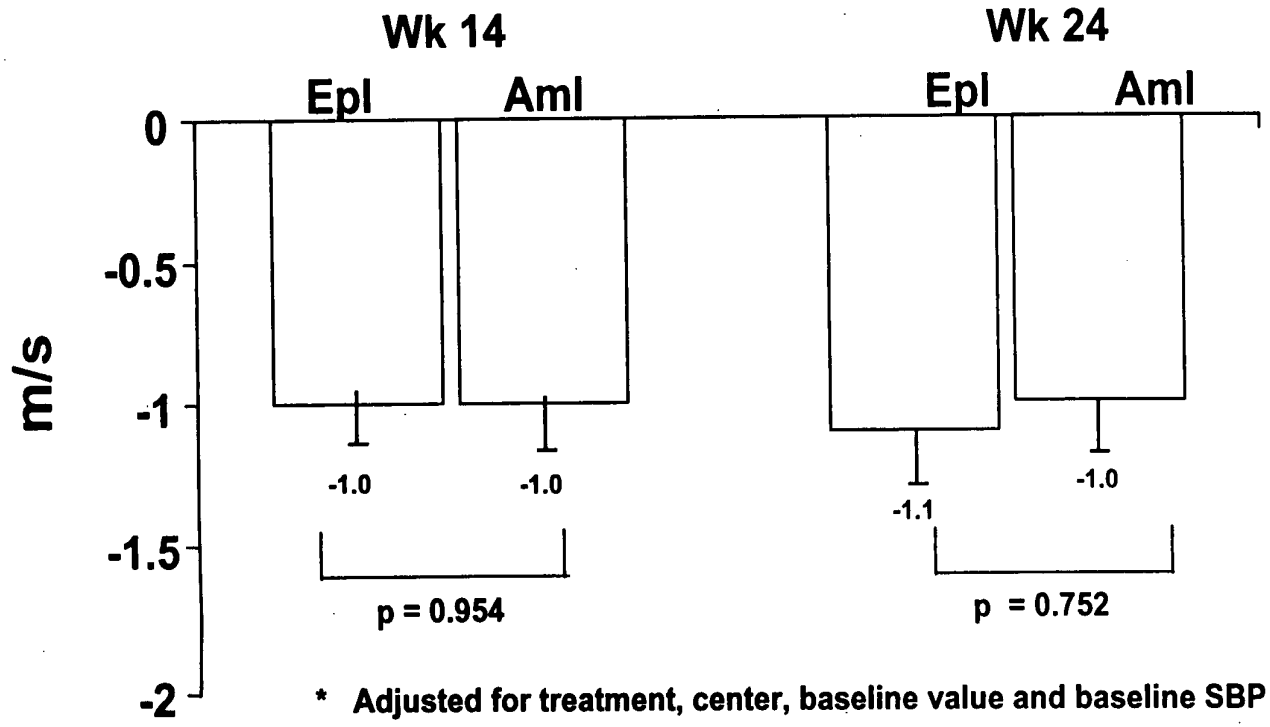


Figure D-37 - Eplerenone vs. Amlodipine in Elevated SBP
Mean Change From Baseline: Carotid-Femoral PWV



* Adjusted for treatment, center, baseline value and baseline SBP

Figure D-38 - Eplerenone vs. Amlodipine in Elevated SBP
Mean Change From Baseline: Carotid-Radial PWV



* Adjusted for treatment, center, baseline value and baseline SBP

Figure D-39 - Eplerenone vs. Amlodipine in Elevated SBP

Adverse Events of Special Interest

AEs [N(%)]	EPL (N = 134)	AMI (135)
Hyperkalemia	2 (1.5)	1 (1.7)
Hyperuricemia	1 (0.7)	0 (0.0)
Increased Lab Values		
GGT	0 (0.0)	0 (0.0)
SGOT	0 (0.0)	0 (0.0)
SGPT	0 (0.0)	0 (0.0)
BUN	0 (0.0)	0 (0.0)
Impotence*	2 (3.3)	0 (0.0)
Gynecomastia	0 (0.0)	0 (0.0)
Hypotension	0 (0.0)	1 (0.7)
Hypokalemia	0 (0.0)	2 (1.5)
Menstrual Irregularities	0 (0.0)	0 (0.0)
Edema Peripheral	6 (4.5)	34 (25.2)

* N = 61 (EPL); 66 (AML)

Figure D-40 - Co-administration with ACE-I or ARB

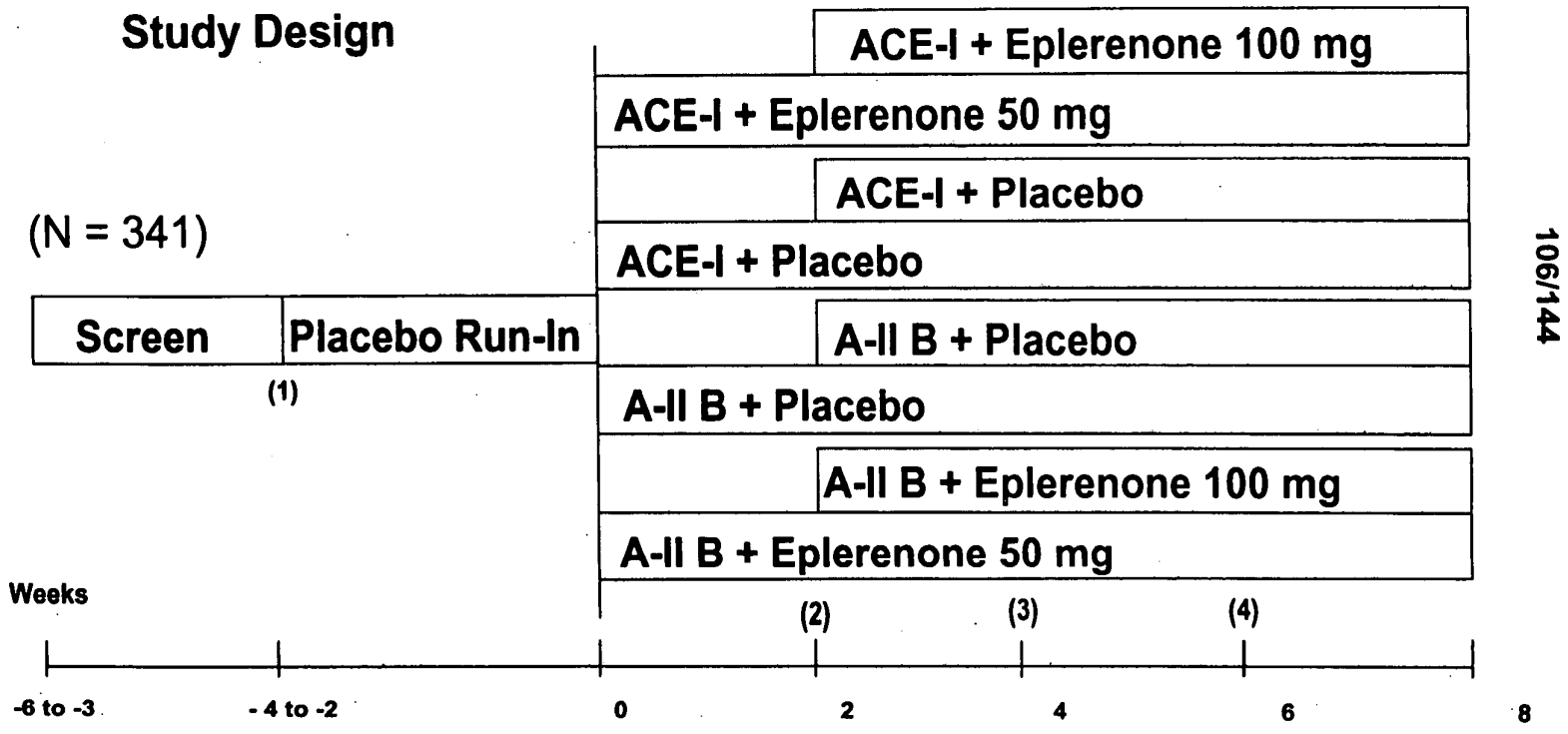
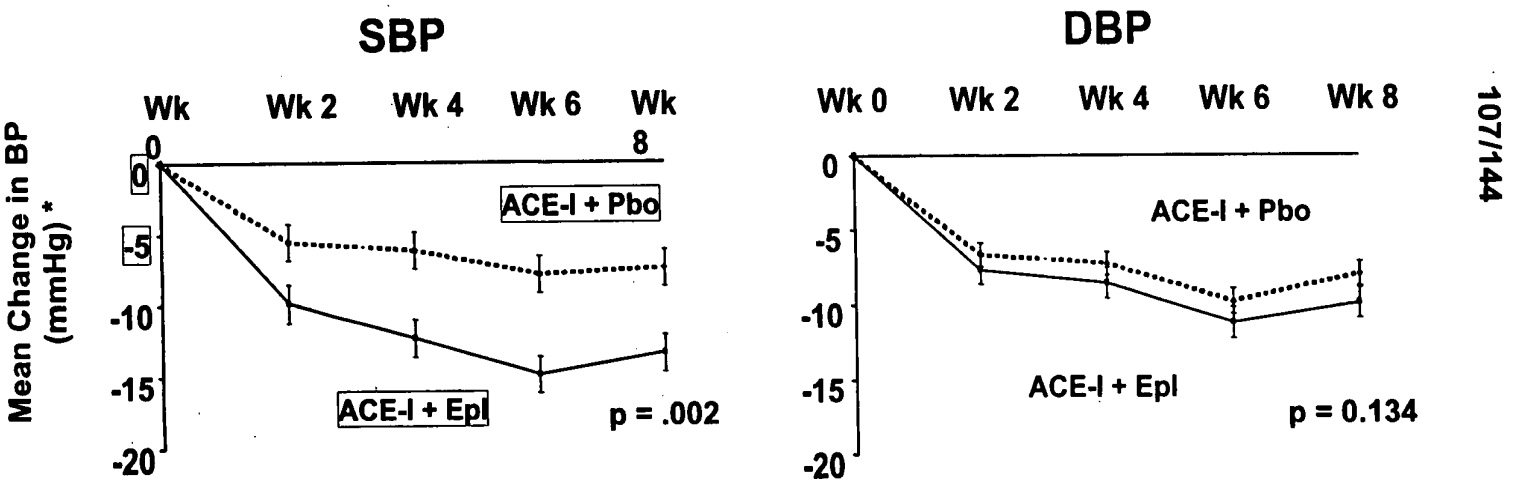


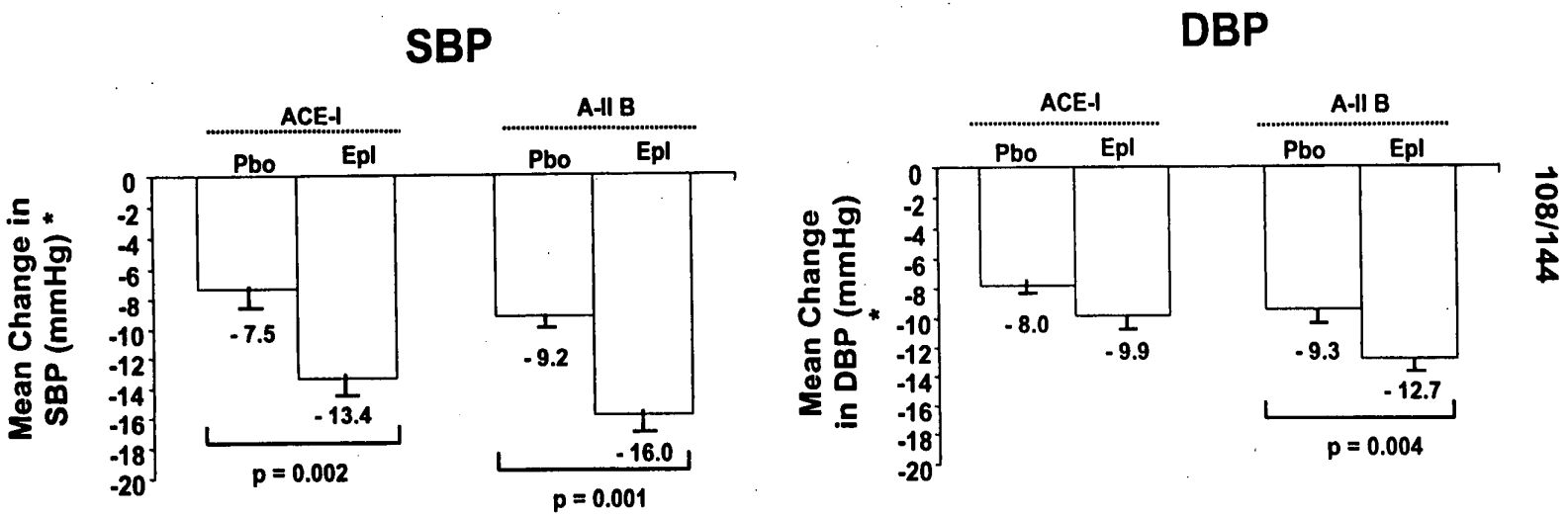
Figure D-41: Mean Change in BP (Each Visit) in Patients not controlled with ACE-I



Adjusted to treatment, center, and baseline value

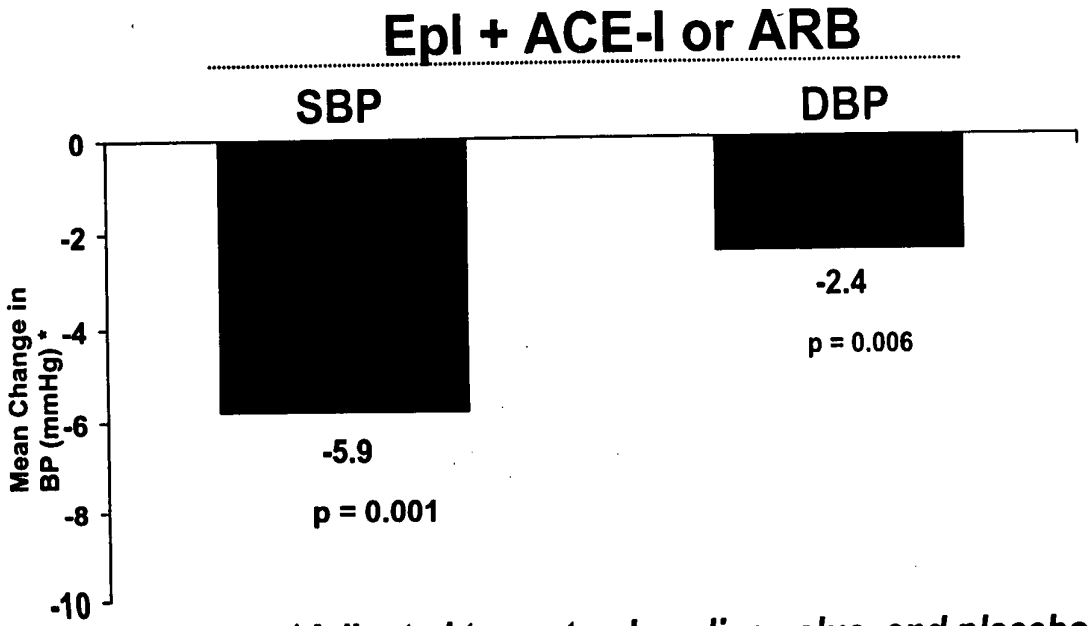
Figure D-42 - Co-Administration with ACE-I or ARB

Mean Change From Baseline in BP
Week 8 (Final Visit)



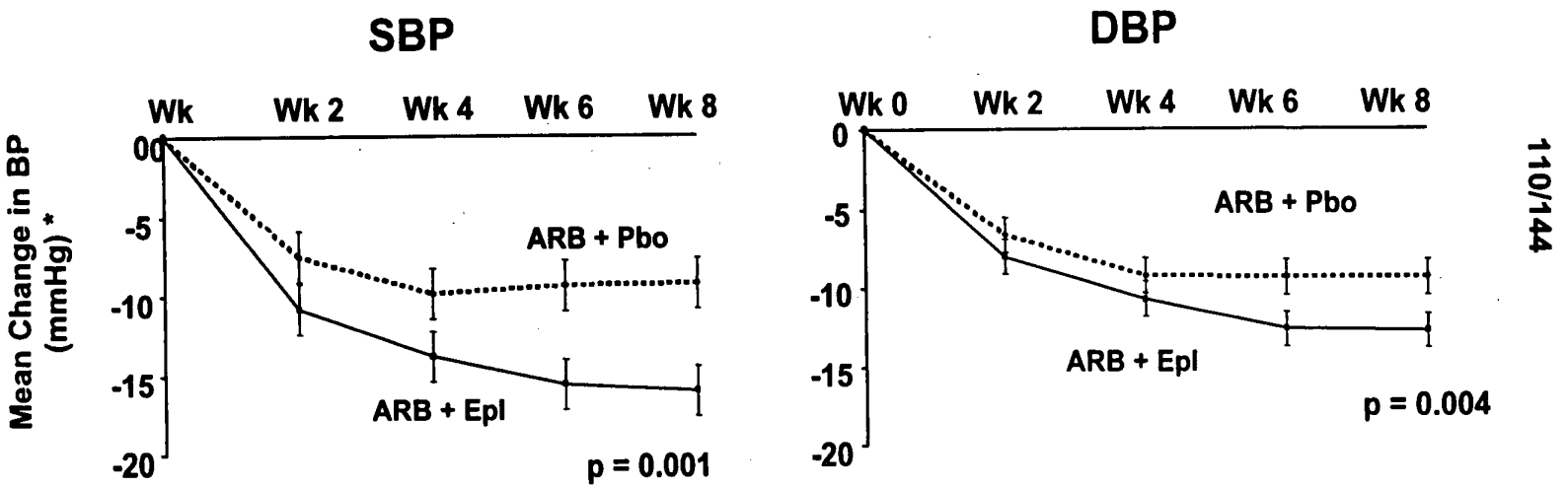
* Adjusted to treatment, center, and baseline value

Figure D-43: Mean Change From Baseline in BP
Week 8 (Final Visit)



*Adjusted to center, baseline value, and placebo-corrected

Figure D-44: Mean Change in BP (Each Visit) in Patients not controlled with ARB



Adjusted to treatment, center, and baseline value

Figure D-45: Mean Change From Baseline: Laboratory Values

	ACE-I		ARB	
Lab Values (Stderr)	Pbo (N = 90)	Epl (N = 87)	Pbo (N = 81)	Epl (N = 83)
AST (SGOT)	0.9 (0.4)	0.6 (0.8)	7.3 (7.0)	0.8 (0.8)
ALT (SGPT)	1.0 (0.8)	1.2 (1.5)	8.1 (8.1)	2.1 (1.1)
Creatinine	1.7 (1.2)	1.0 (1.2)	0.4 (1.3)	4.4 (1.5)
BUN	-0.02 (0.14)	0.06 (0.15)	0.02 (0.19)	0.73 (0.20)*
Na	0.3 (0.3)	-0.6 (0.3)	0.2 (0.4)	-0.7 (0.4)
K*	0.03 (.04)	0.13 (0.05)	0.04 (0.04)	0.20 (0.05)*
Uric Acid	2.3 (5.4)	11.3 (7.0)	-1.8 (5.0)	25.4 (7.3)*
Mg	0.002 (0.008)	-0.003 (0.008)	-0.003 (0.007)	-0.013 (0.009)

* p < 0.001 vs. A-II /Pbo

Figure D-46: Change in Serum Potassium Values in Patients not controlled with ACE-I

	ACE-I + Pbo			ACE-I + Epl		
	N	Baseline	Mean Change	N	Baseline	Mean Change
Week 2	88	4.36	0.04	82	4.30	0.10
Week 4	84	4.36	0.02	77	4.34	0.15
W k 6	77	4.36	0.09	71	4.32	0.16
Week 8	55	4.38	0.03	59	4.32	0.13

Figure D-47: Change in Serum Potassium Values in Patients not controlled with ARB

	ARB + Pbo			ARB + Epl		
	N	Baseline	Mean Change	N	Baseline	Mean Change
Week 2	78	4.29	0.01	82	4.31	0.18
Week 4	76	4.29	0.01	79	4.31	0.19
Week 6	72	4.29	0.01	68	4.33	0.21
Week 8	58	4.26	0.04	62	4.31	0.20

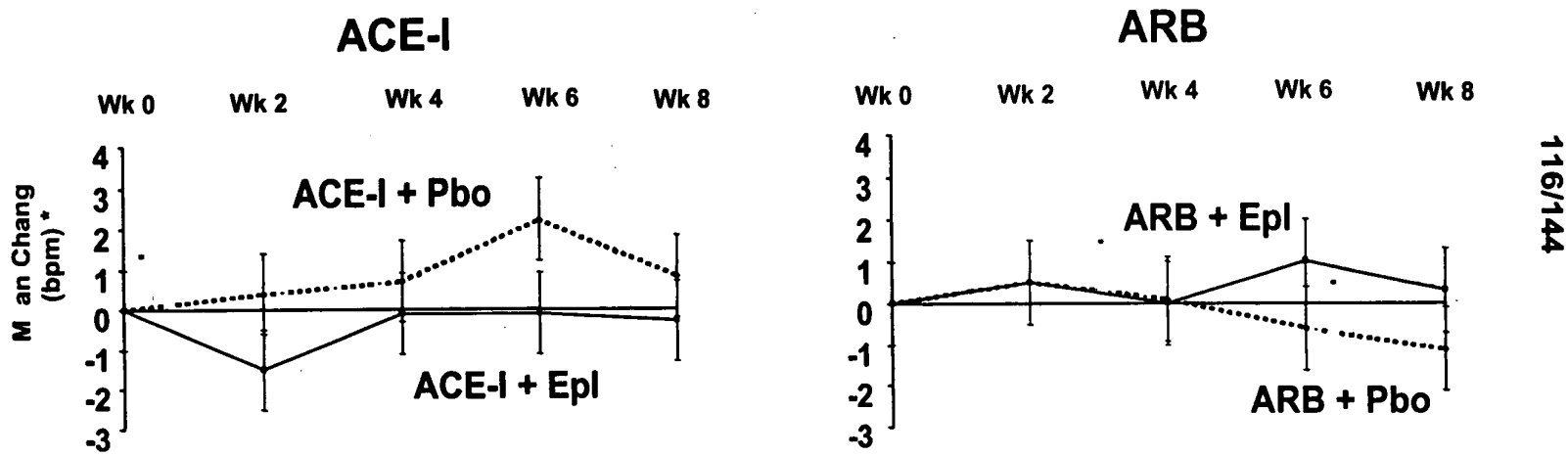
Figure D-48: Adverse Events of Interest

[N (%)]	ACE-I Pbo (N = 90)	ACE-I Epl (N = 87)	ARB Pbo (N = 81)	ARB Epl (N = 83)
Aggravated Hypertension	0	1 (1.1)	0	0
Hyperkalemia	0	1 (1.1)	0	0
Hyperuricemia	0	1 (1.1)	0	2 (2.4)
Increased Lab Values				
GGT	0	1 (1.1)	1 (1.2)	0
SGOT	0	1 (1.1)	1 (1.2)	0
SGPT	0	1 (1.1)	1 (1.2)	1 (1.2)
BUN	0	0	0	1 (1.2)
Impotence	0	0	0	1 (2.4)
Gynecomastia	0	0	0	0
Hypotension	0	0	0	1 (1.2)
M nstrual Abnormalities	0	0	0	0

Figure D-49: Serious Adverse Events

	ACE-I		ARB	
	Pbo (N = 90)	Epl (N = 87)	Pbo (N = 81)	Epl (N = 83)
Sudden Death	0	1	0	0
Aggravated HTN	0	1	0	0
Syncope	1	0	0	0
Inguinal Hernia	0	1	0	0

Figure D-50: *Mean Change in Heart Rate (Each Visit)*



**Adjusted to treatment, center, and baseline value*

Figure D-51: Mean Active Renin and Aldosterone Levels

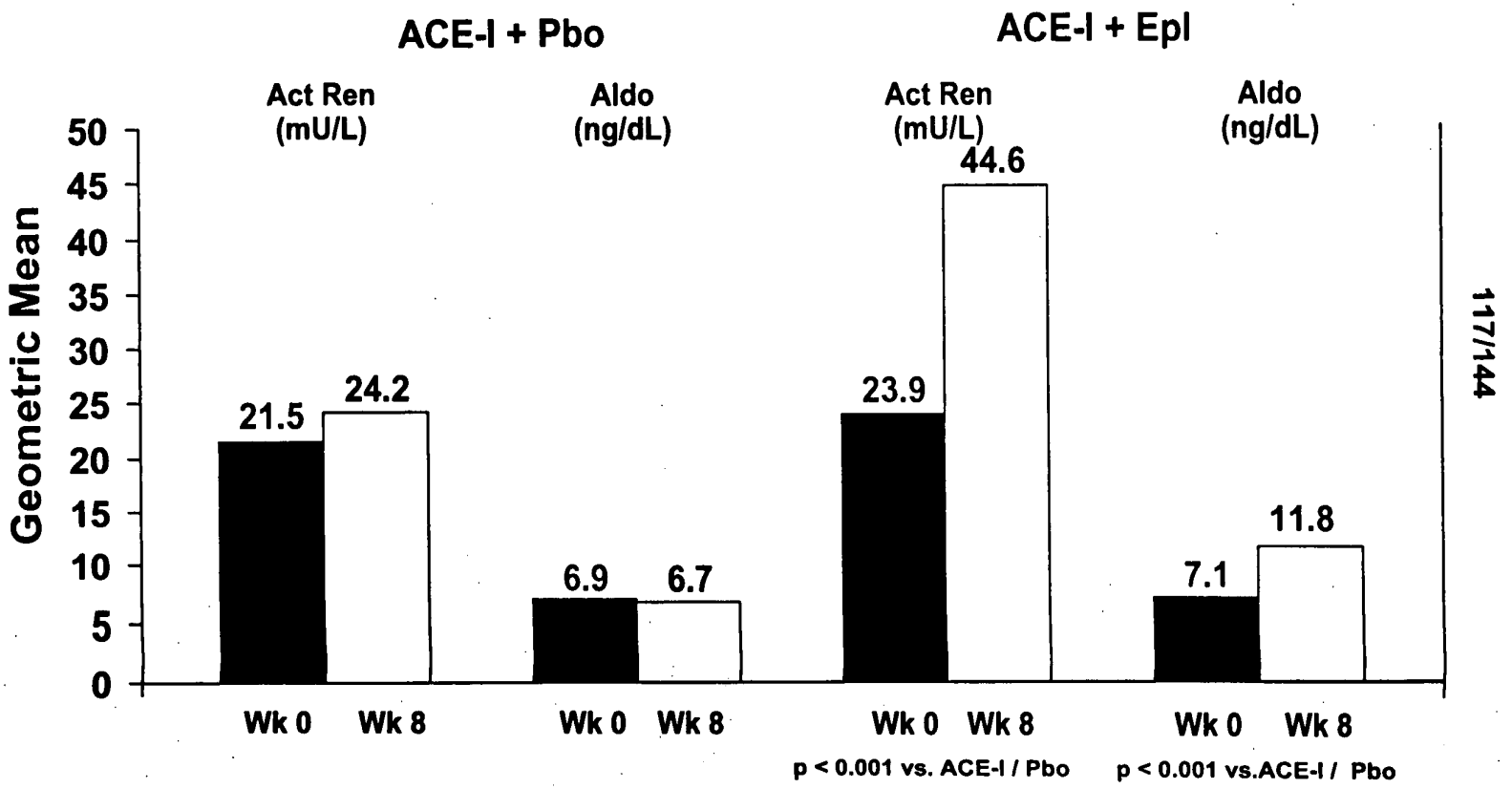


Figure D-52: Mean Active Renin and Aldosterone Levels

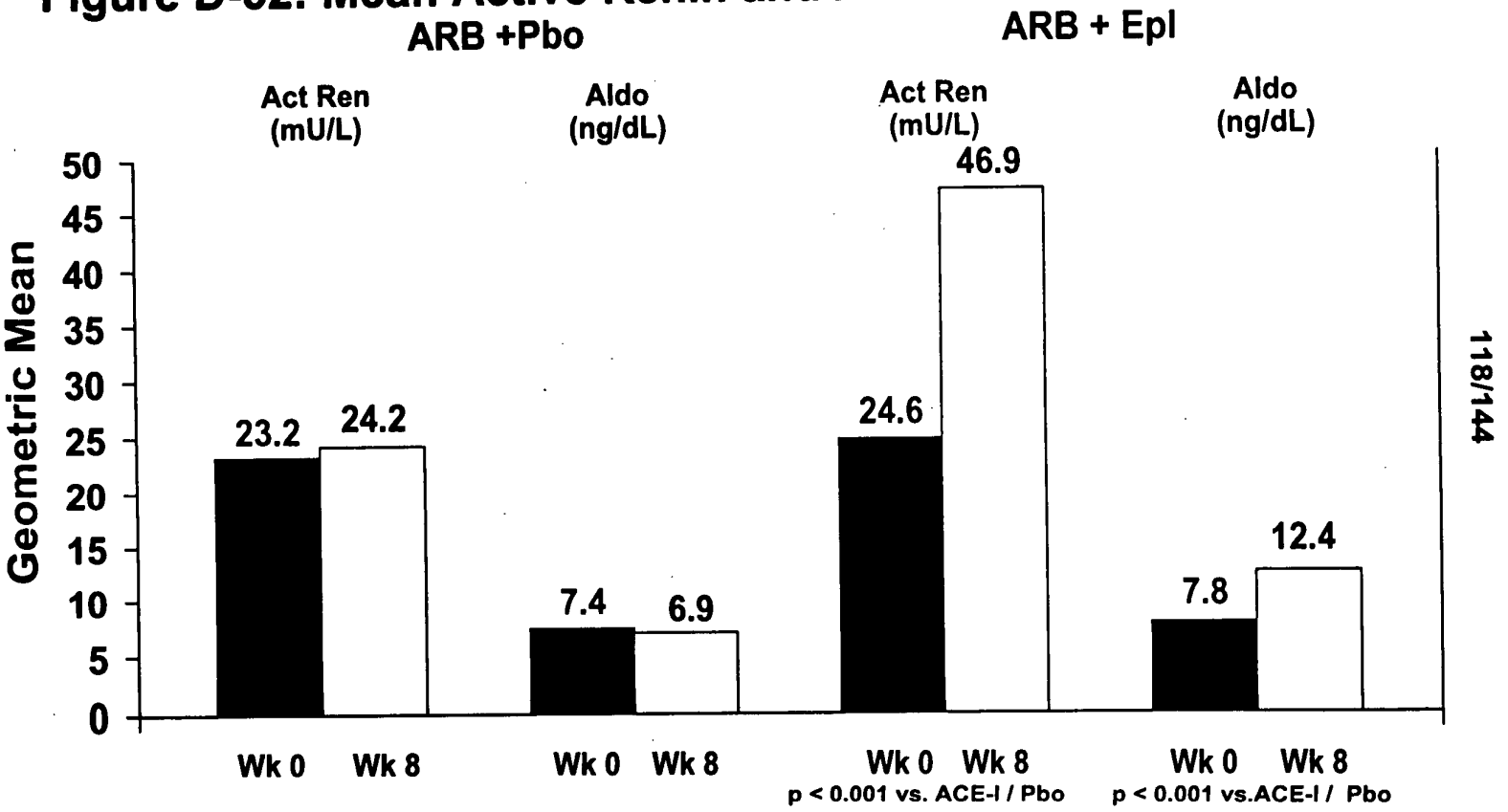


Figure D-53: Reason For Withdrawal

	ACE-I		ARB	
[N (%)]	Pbo (N = 90)	Epl (N = 87)	Pbo (N = 81)	Epl (N = 83)
Adverse Event	2 (2.2)	2 (2.3)	0 (0.0)	1 (1.2)
Treatment Failure	26 (28.9)	15 (17.2)	17 (21.0)	8 (9.6)
Lost to Follow-up	0 (0.0)	3 (3.4)	0 (0.0)	1 (1.2)
Protocol Non-Compliance	1 (1.1)	1 (1.1)	0 (0.0)	3 (3.6)
Pre-Existing Violation	1 (1.1)	4 (4.6)	0 (0.0)	0 (0.0)
Oth r	2 (2.2)	1 (1.1)	2 (2.5)	4 (4.8)

Figure D-54: Percent of Patients Responding to Treatment: DBP

	ACE-I			ARB		
Week	Pbo (N = 89)	Epl (N = 85)	% Difference	Pbo (N = 80)	Epl (N = 82)	% Difference
2	44.9	47.6	2.7	48.8	54.9	6.1
4	46.1	57.6	11.5	67.5	74.4	6.9
6	60.7	72.9	12.2	71.3	90.2	18.9
8 (Final)	55.1	62.4	7.3	73.8	87.8	14.0

Note: Responder defined as seDBP < 90 mmHg or > 90 but a ≥ 10 mmHg reduction from baseline

Figure D-55 - Co-administration with CCB and β-Blocker

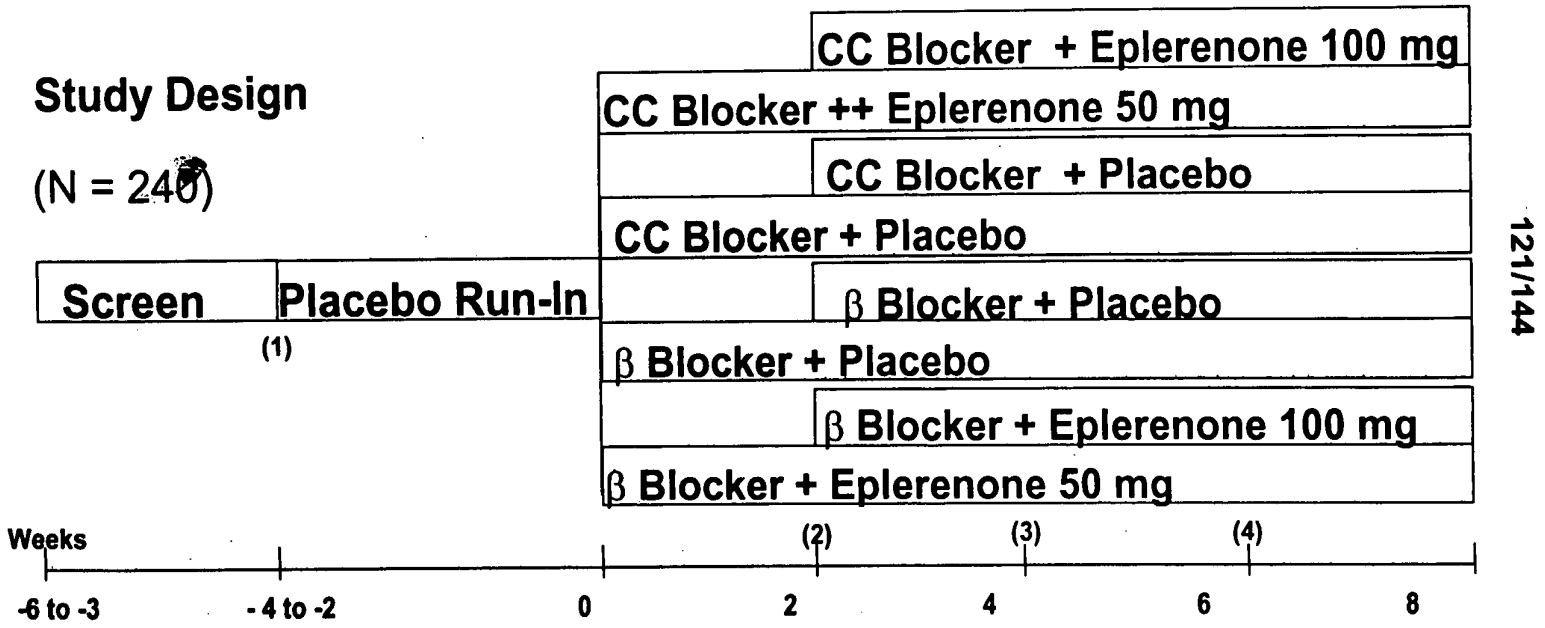
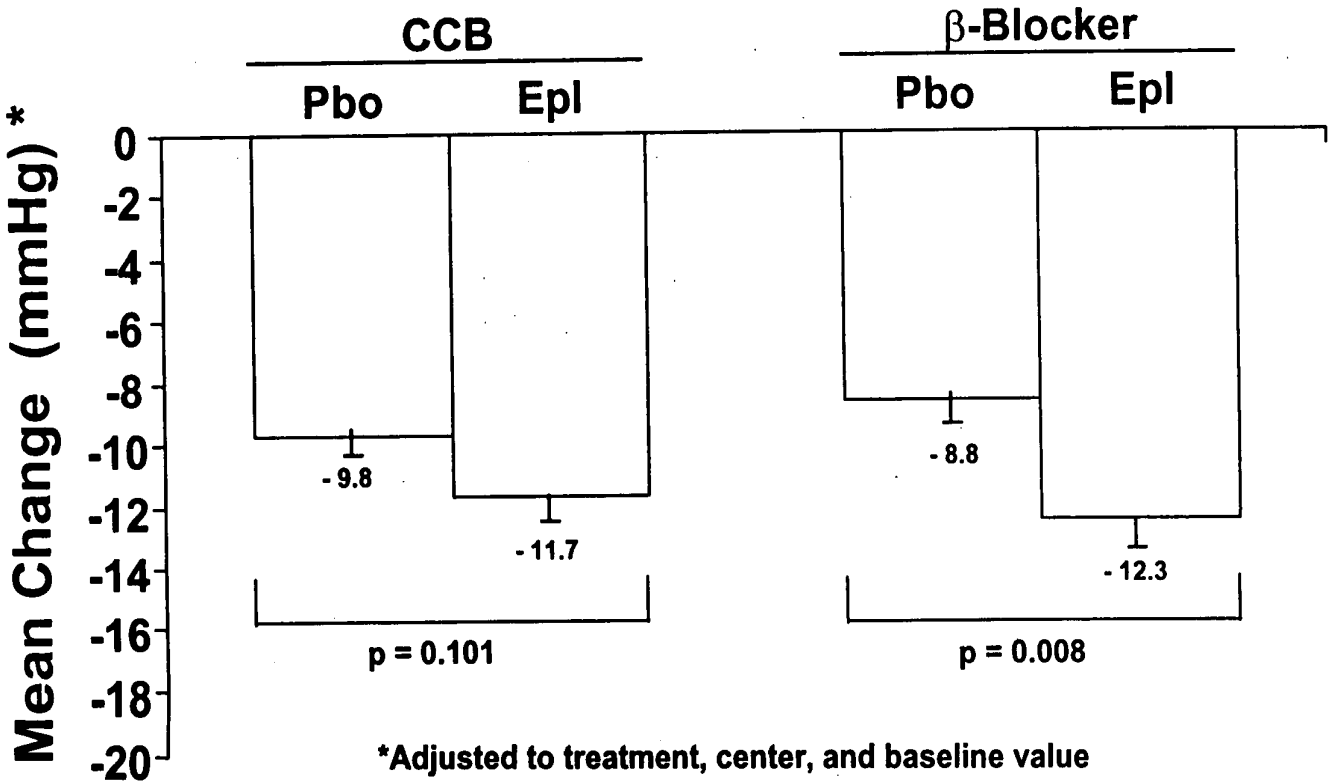


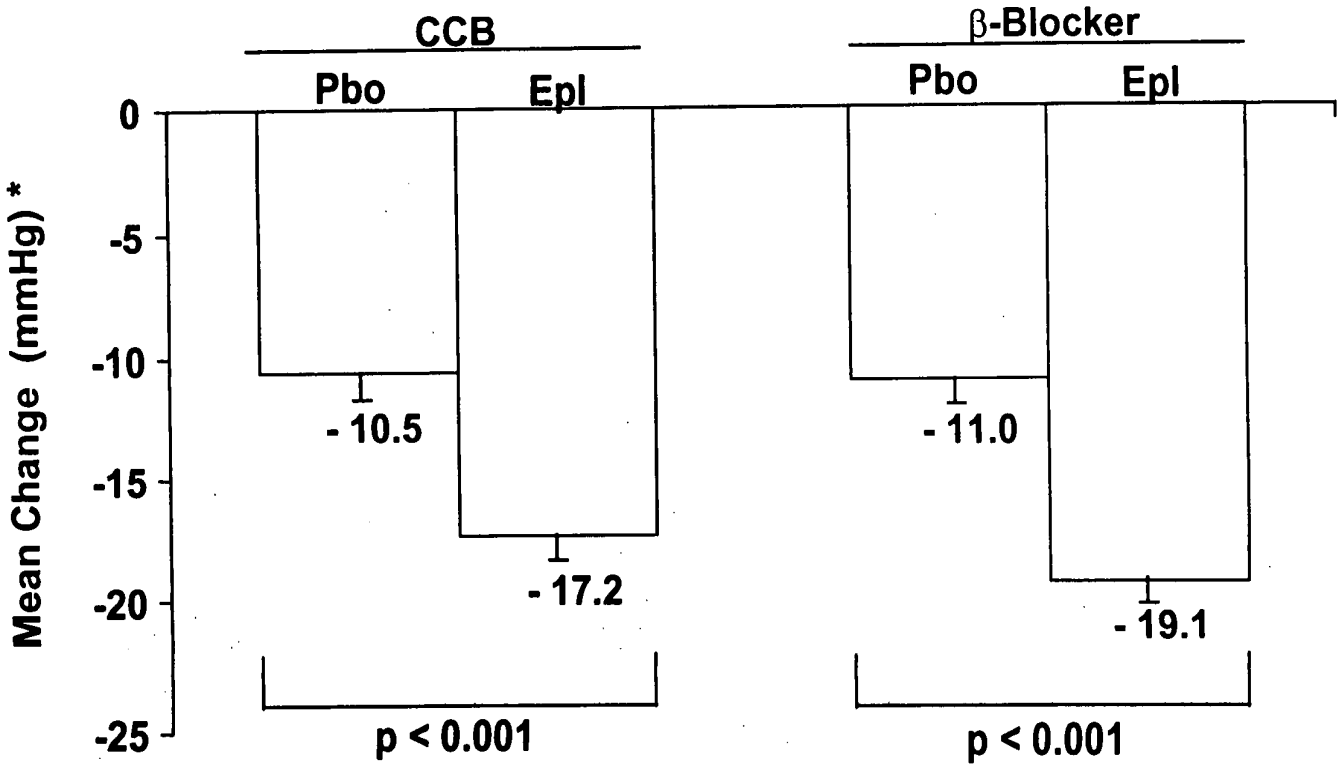
Figure D-56 - Co-Administration with CCB or β-Blocker

Mean Change in DBP: Baseline vs. Final Visit



*Adjusted to treatment, center, and baseline value

Figure D-57 - Co-Administration with CCB or β-Blocker
Mean Change in SBP: Baseline vs. Final Visit



*Adjust d to treatment, center, and baseline value

Figure D-58 - Co-Administration with CCB or β-Blocker

Adverse Events of Special Interest

Adverse Events	CCB		β-Blocker	
	Pbo (N = 67)	Epl (N = 70)	Pbo (N = 66)	Epl (N = 69)
Hyp rkalemia	0	0	0	4
Hyperuricemia	0	0	0	0
Increased Lab Values				
GGT	0	0	0	0
SGOT	0	0	0	0
SGPT	1	0	0	0
BUN	0	0	0	0
Impotence	0	0	0	0
Gynecomastia	0	0	0	0
Menstrual Abnormalities	0	0	0	0
Hypotension	0	1	0	0

Figure D-59 - Long-Term, Open Label Safety Study Design

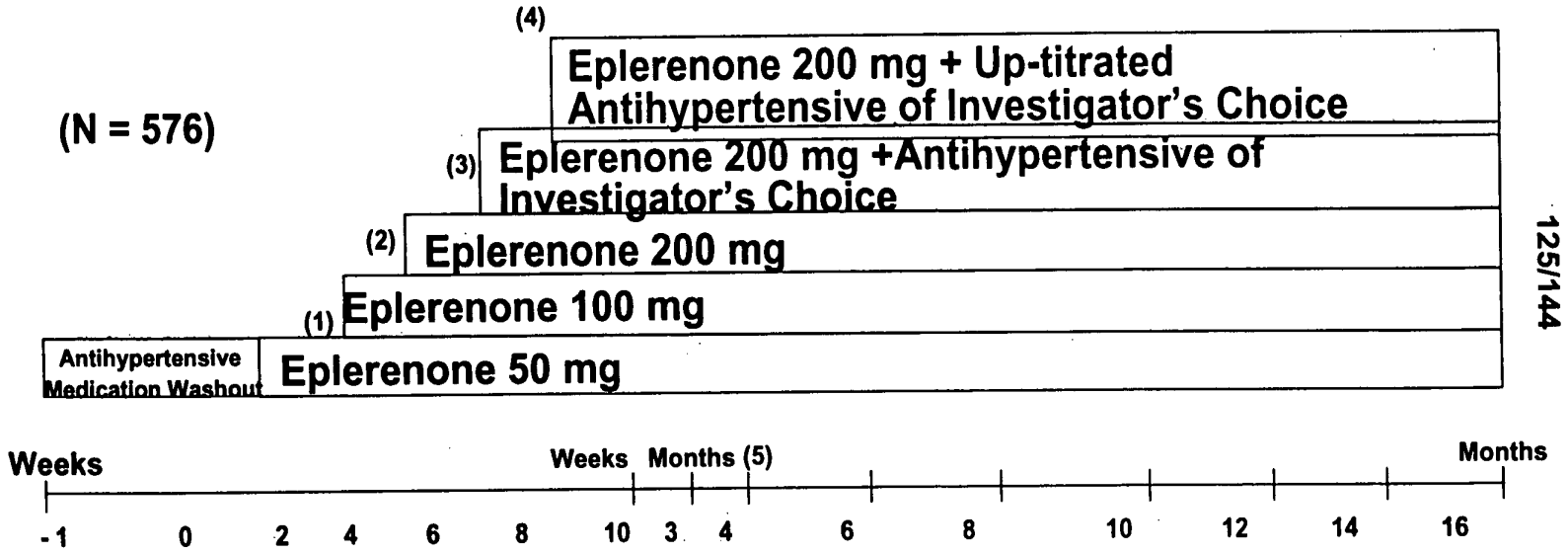
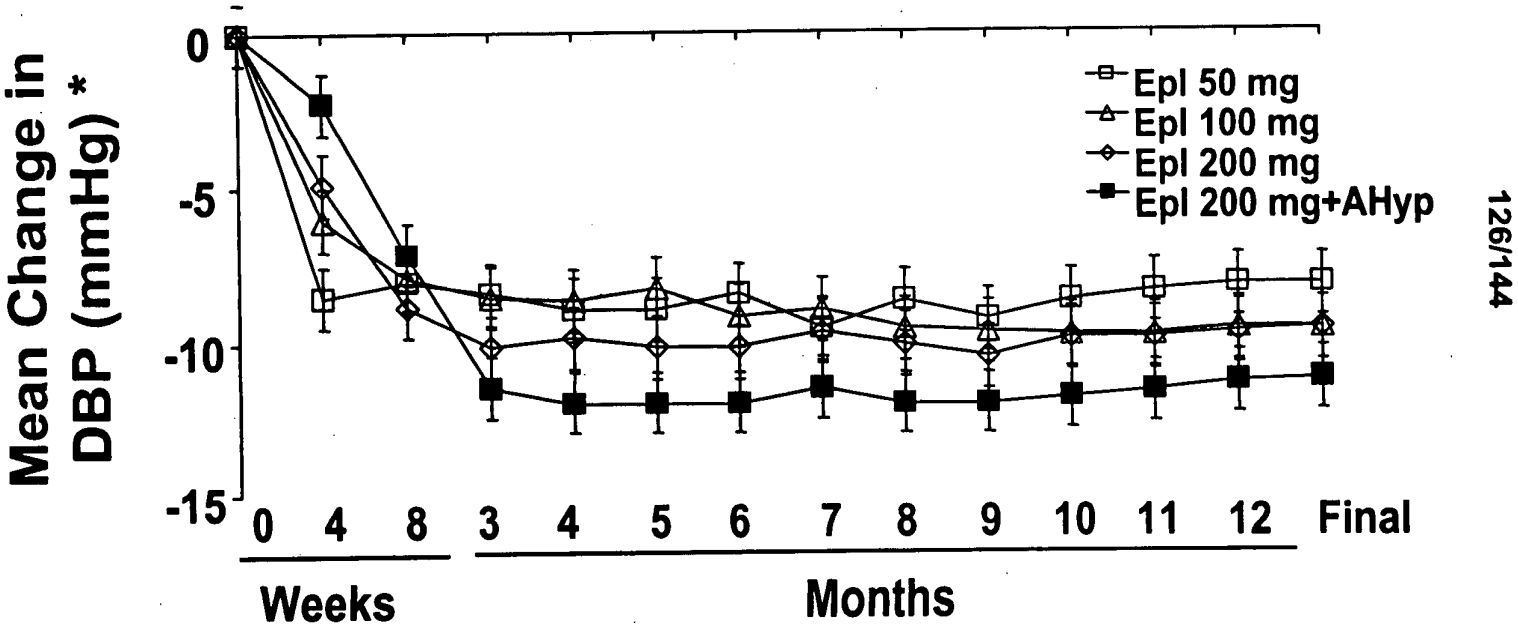


Figure D-60 - Long-Term Open Label Safety

Mean Change in DBP

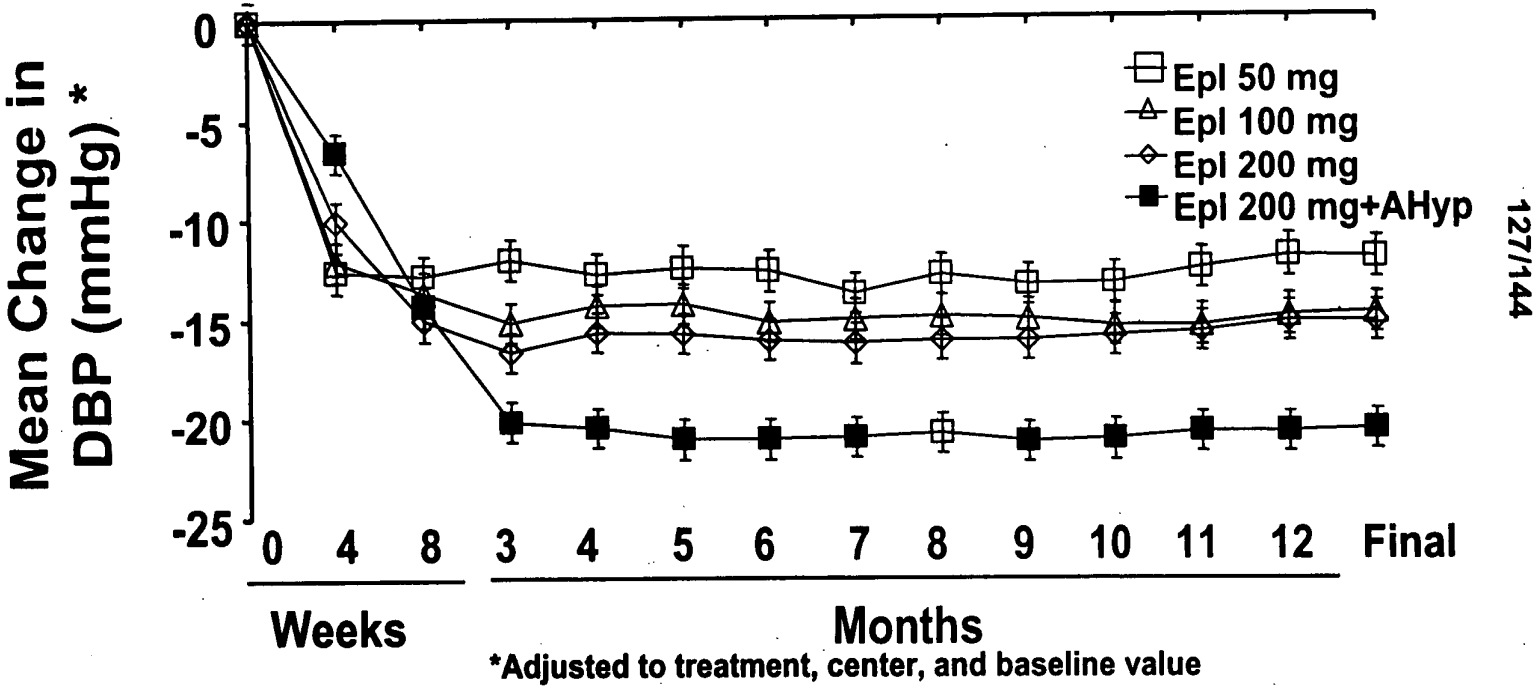


*Adjusted to treatment, center, and baseline value

126/144

Figure D-61 - Long-Term Open Label Safety

Mean Change in SBP



*Adjusted to treatment, center, and baseline value

Figure D-62 - Long-Term Open Label Safety

Adverse Events of Special Interest

Adverse Event Incidence (Rate)	Eplerenone Doses				
	Combined	50 mg	100 mg	200 mg	200 + AHyp
Impot nce*	9 (3.0)	2	2	1	4
Gynecomastia	2 (0.3)				2
Hypotension	2 (0.3)				2
Menstrual Abnormalities*	3 (1.1)	2		1	
Hyperkalemia	8 (1.4)			6	2

* N =284 (Menstrual Disorder); N = 302 (Impotence)

Figure D-63 - Eplerenone vs. Amlodipine in ABPM Study Design

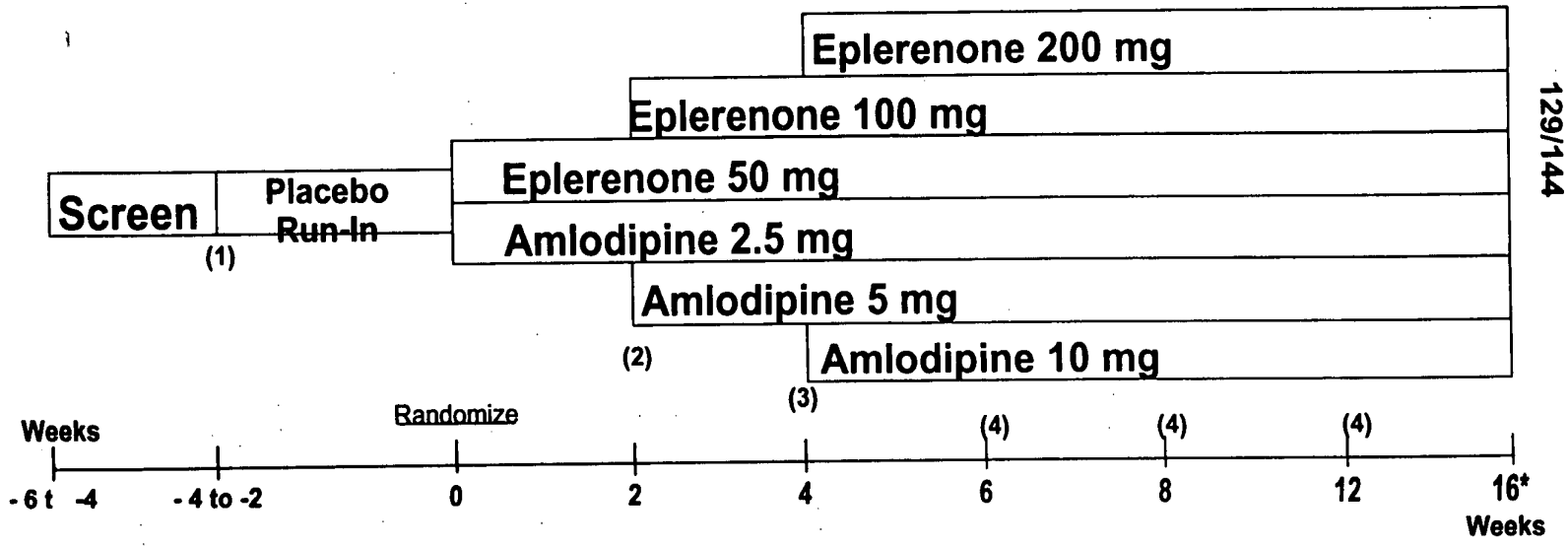


Figure D-64 - Eplerenone vs. Amlodipine in ABPM

DBP: Mean Change From Baseline (ABPM)

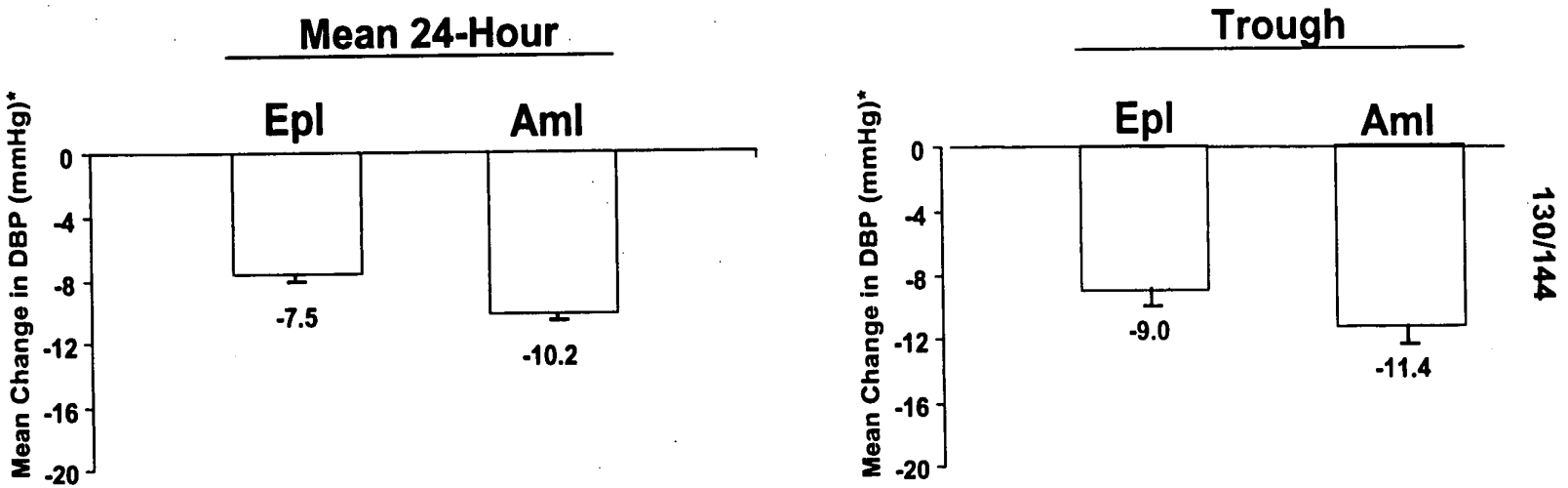
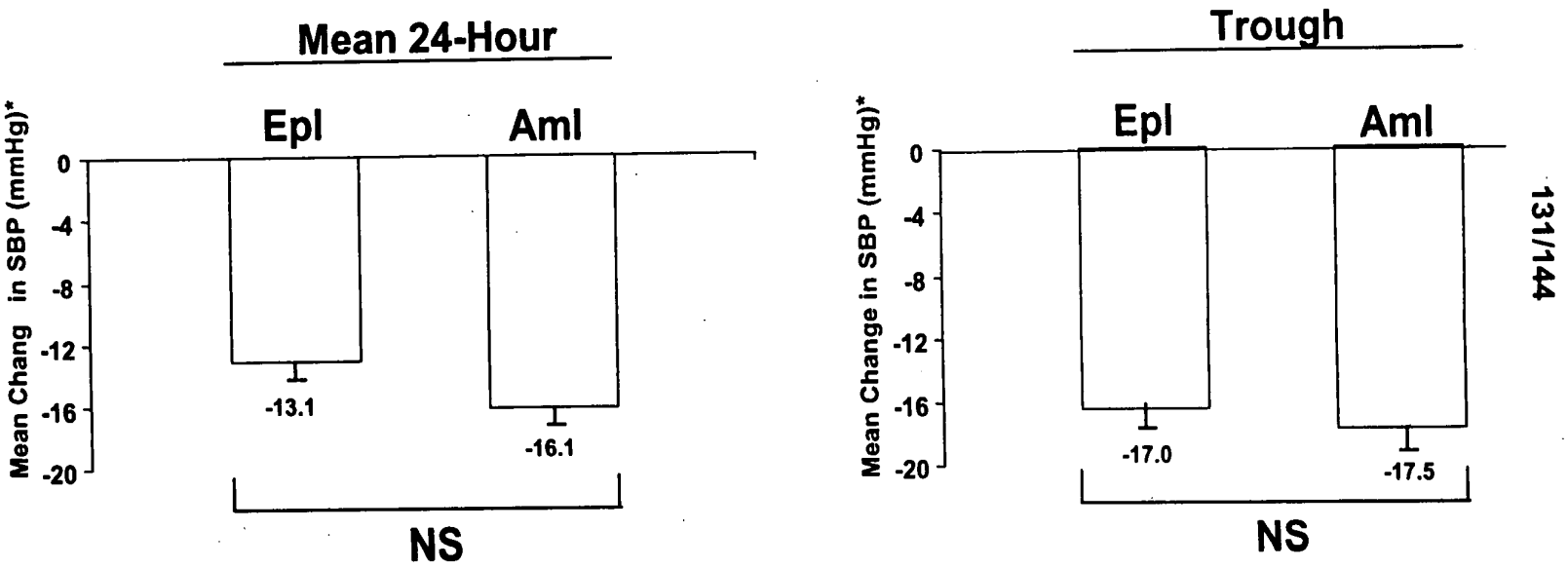


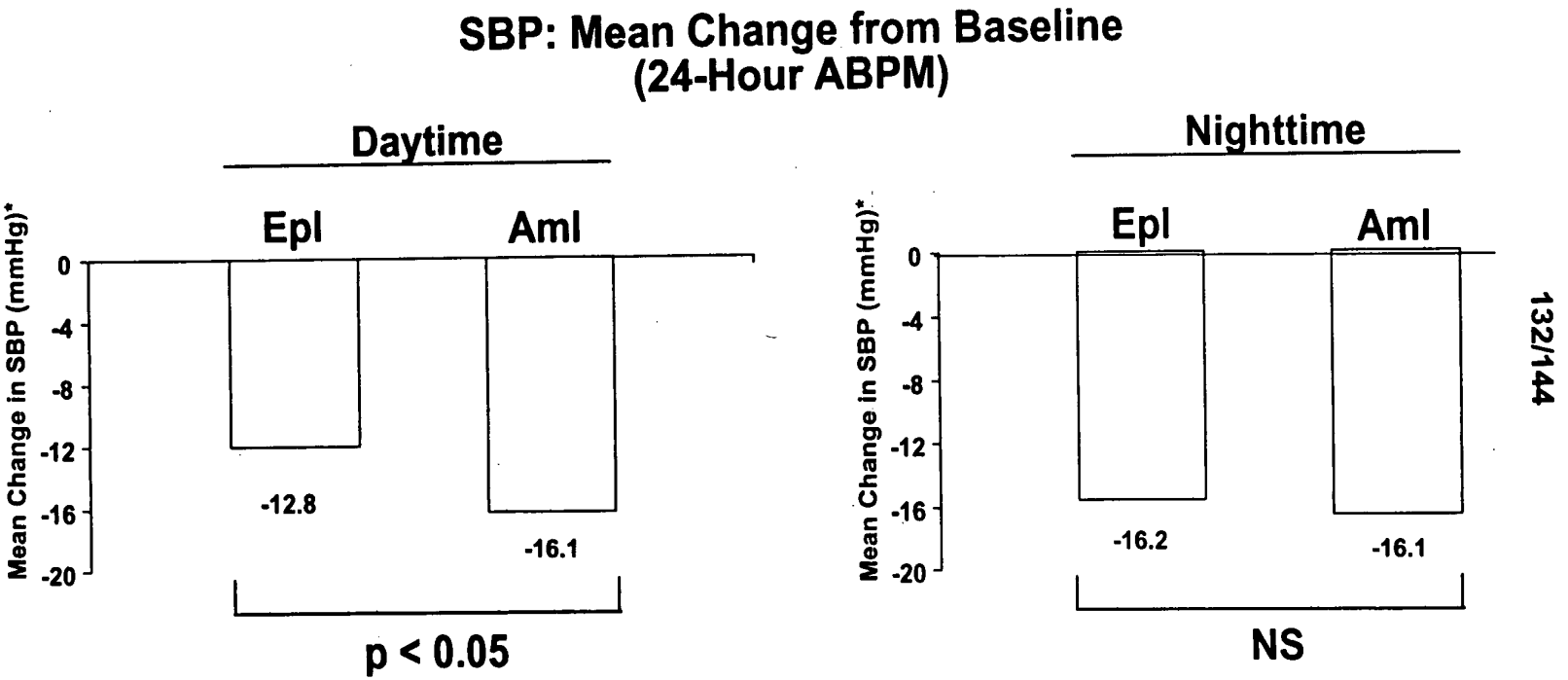
Figure D-65 - Eplerenone vs. Amlodipine in ABPM

SBP: Mean Change From Baseline (ABPM)



* Adjusted to treatment, center, and baseline value

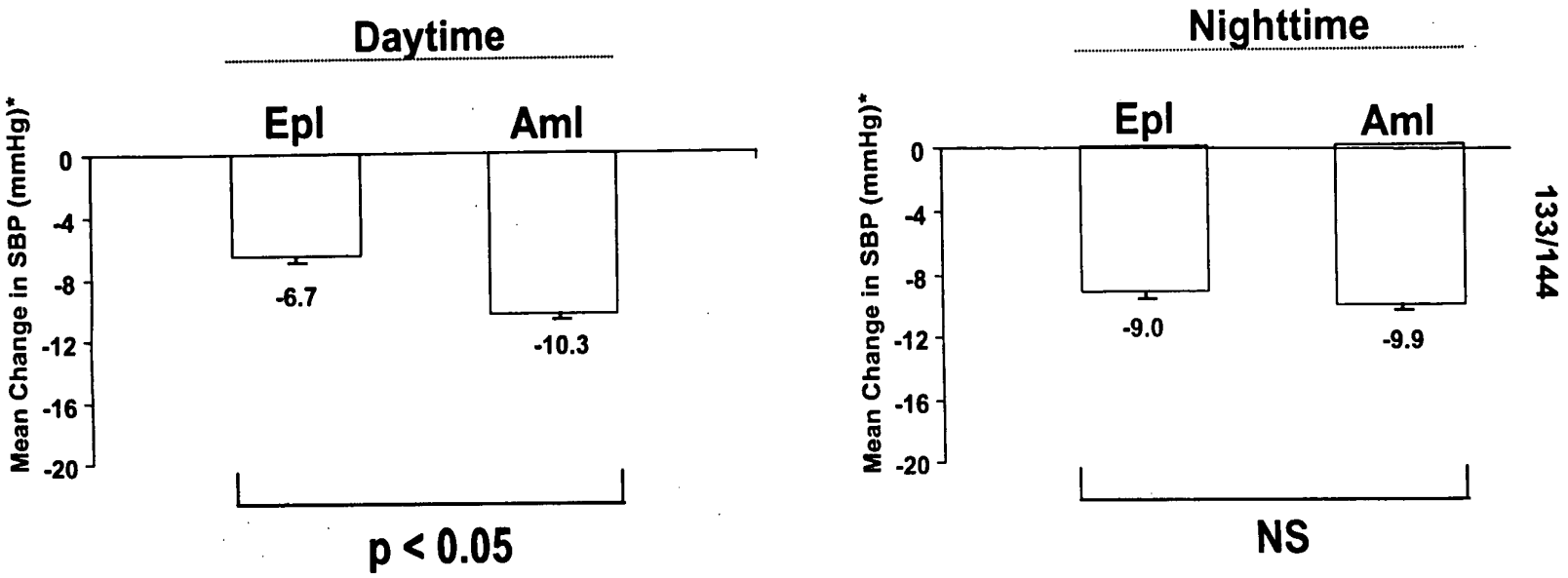
Figure D-66 - Eplerenone vs. Amlodipine in ABPM



* Adjusted to treatment, center, and baseline value

Figure D-67 - Eplerenone vs. Amlodipine in ABPM

DBP: Mean Change from Baseline (24-Hour ABPM)



* Adjusted to treatment, center, and baseline value

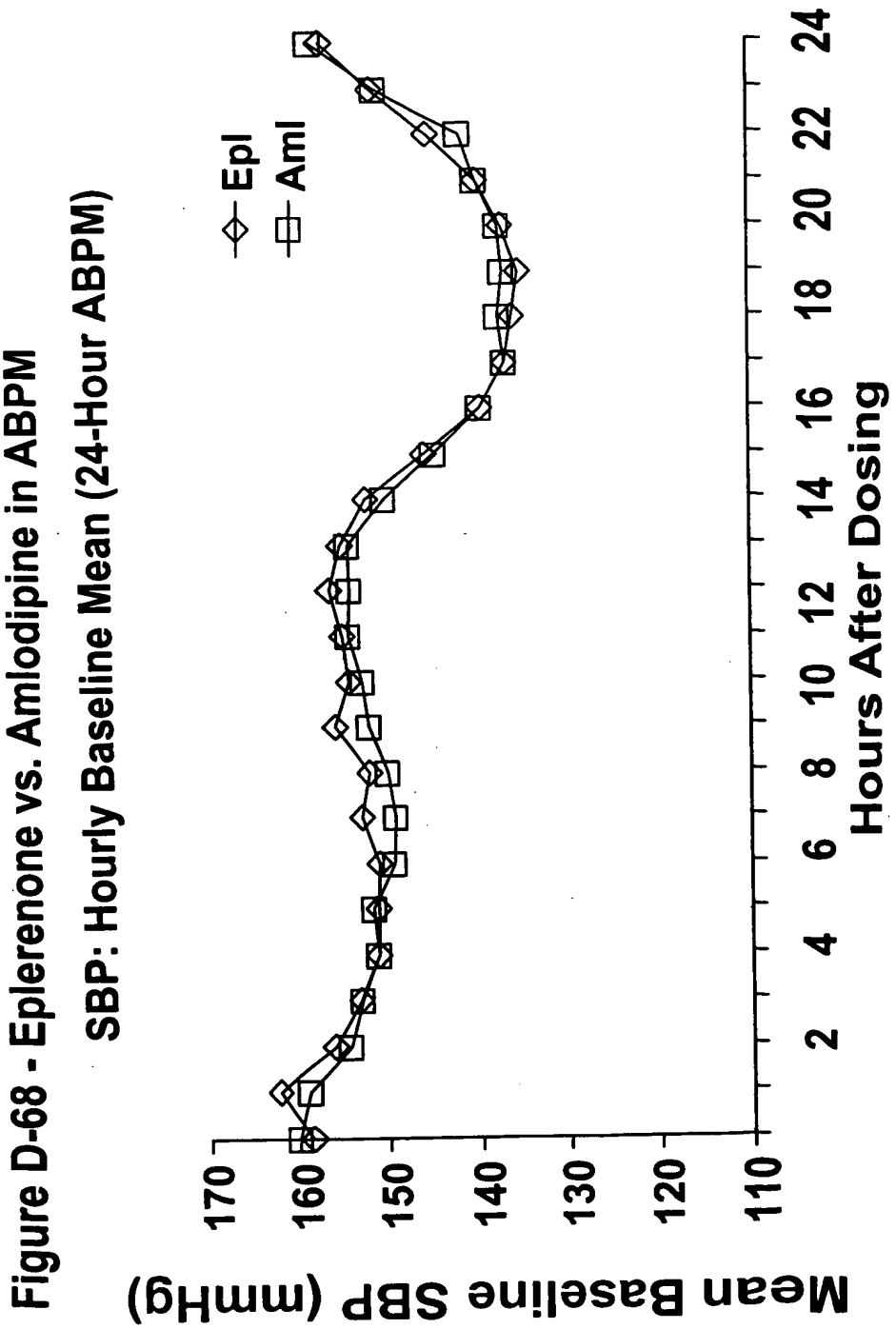


Figure D-68 - Eplerenone vs. Amlodipine in ABPM
SBP: Hourly Baseline Mean (24-Hour ABPM)

Figure D-69 - Eplerenone vs. Amlodipine in ABPM

DBP: Hourly Baseline Mean (24-Hour ABPM)

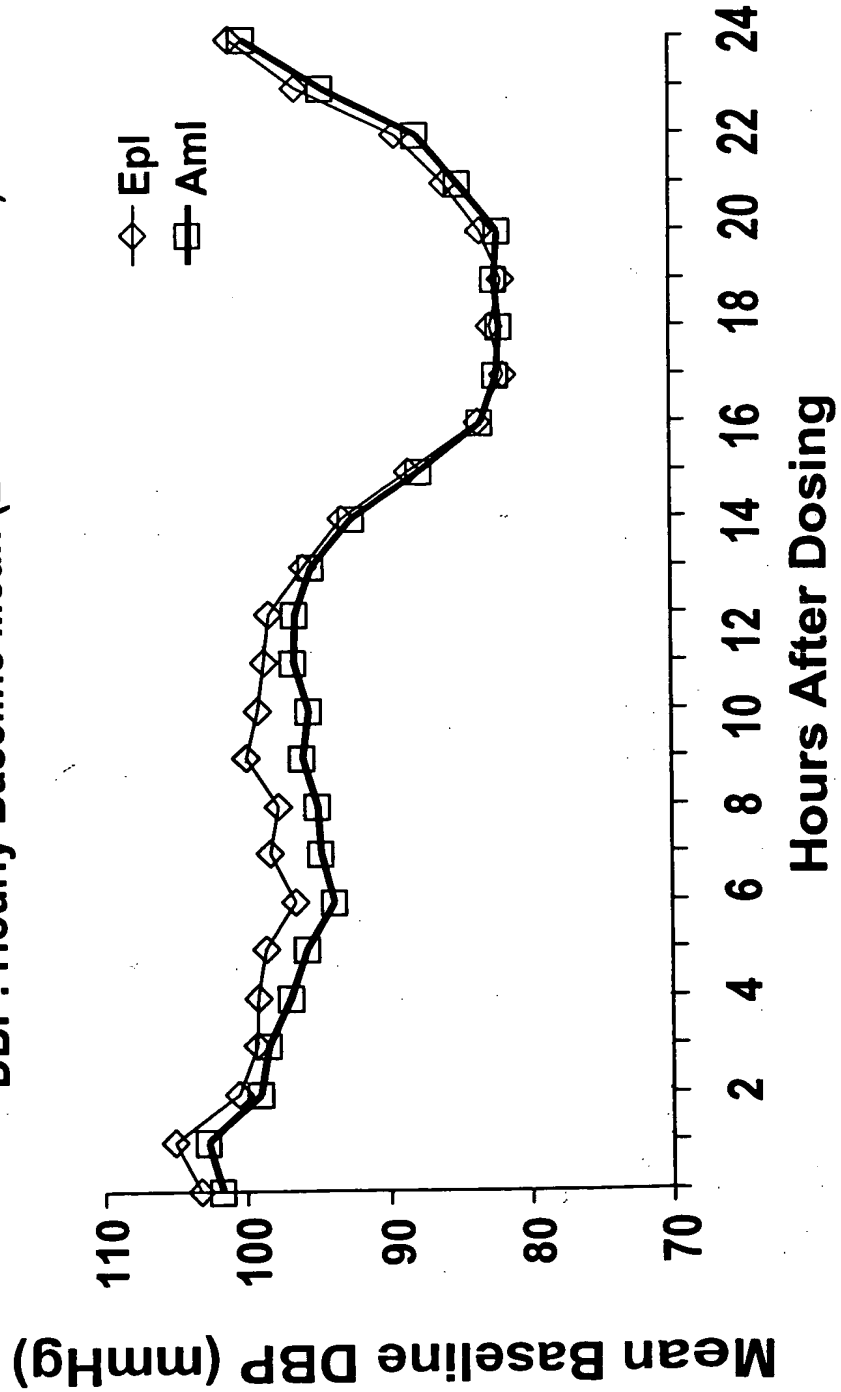


Figure D-70 - Eplerenone vs. Amlodipine in ABPM

SBP: Hourly Endpoint Mean (24-Hour ABPM)

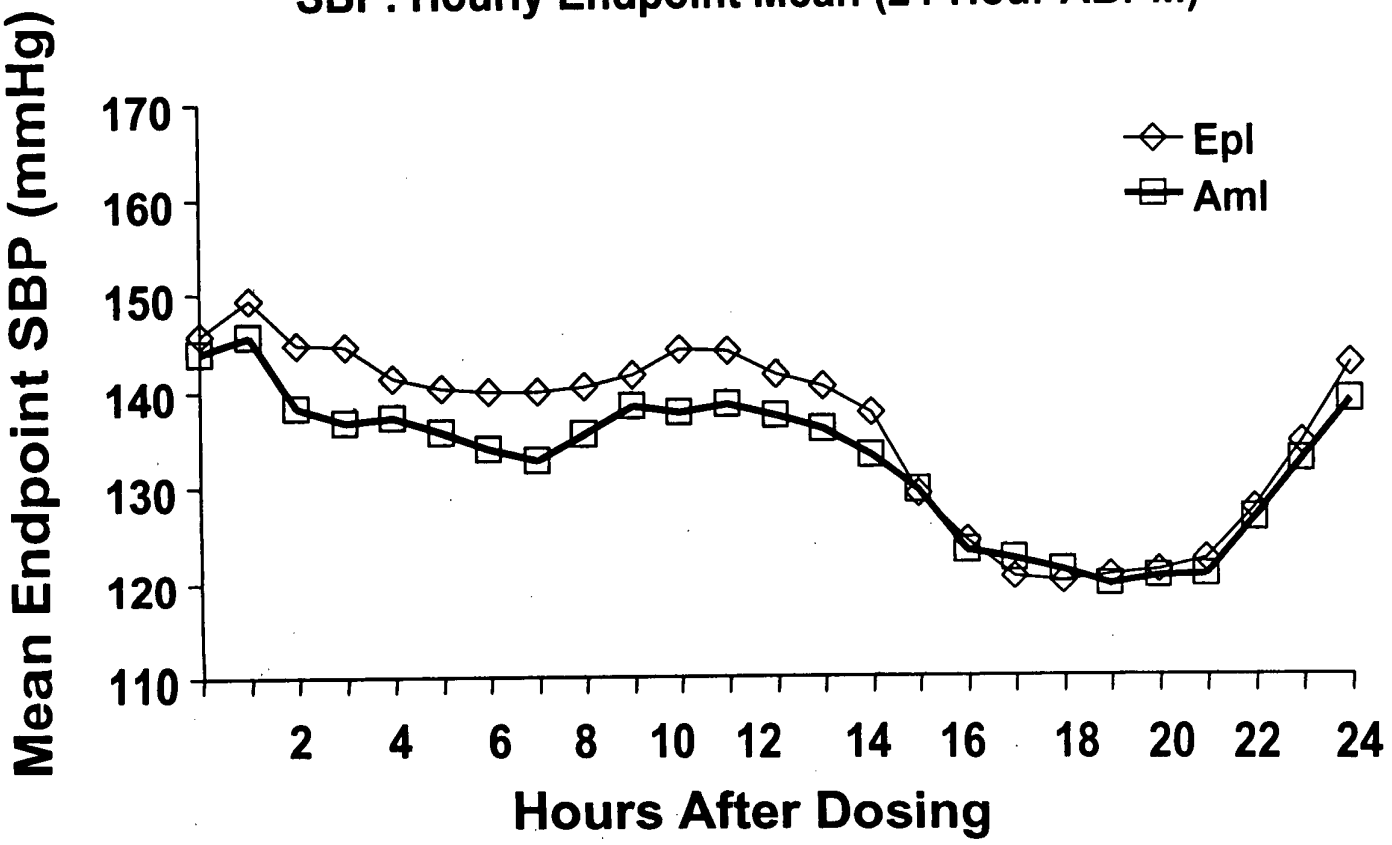


Figure D-71 - Eplerenone vs. Amlodipine in ABPM

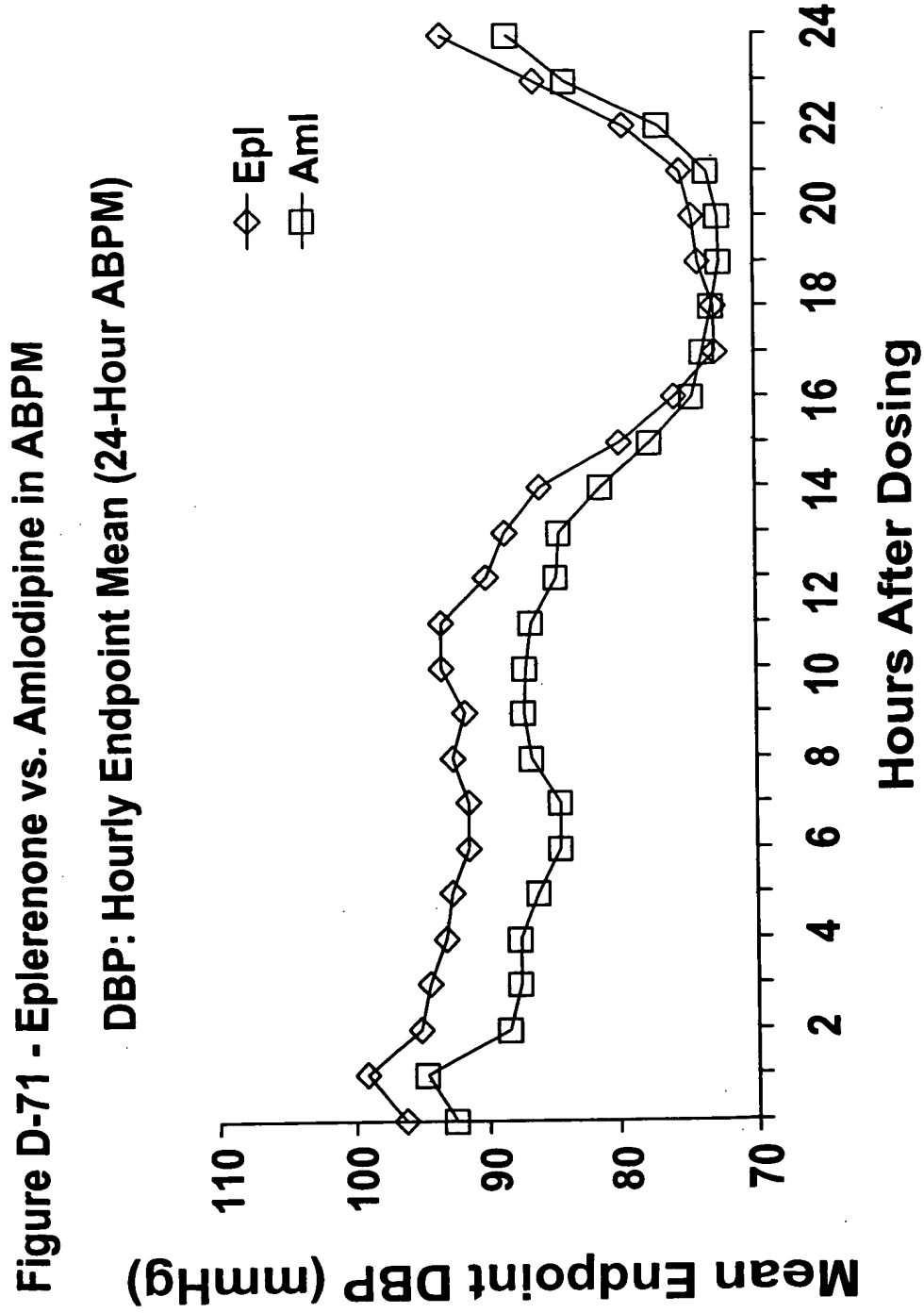


Figure D-72 - Eplerenone vs. Amlodipine in ABPM

Adverse Events of Special Interest

AEs [N(%)]	Eplerenone (N=88)	Amlodipine (N=91)
Edema Peripheral	0 (0.0)	11 (12.1)
Hyperkalemia	0 (0.0)	0 (0.0)
Hyperuricemia	0 (0.0)	0 (0.0)
Increased Lab Values		
GGT	0 (0.0)	0 (0.0)
SGOT	0 (0.0)	0 (0.0)
SGPT	0 (0.0)	0 (0.0)
BUN	0 (0.0)	0 (0.0)
Impotence*	1 (2.2)	0 (0.0)
Gynecomastia*	1 (2.2)	0 (0.0)
Hypotension	0 (0.0)	0 (0.0)
Hypokalemia	0 (0.0)	1 (1.1)
Menstrual Abnormalities**	0 (0.0)	0 (0.0)

* N = 46 (EPL); 56 (AML) ** N = 42 (Epl); 35 (Aml)

Figure D-73 - Study Schematic

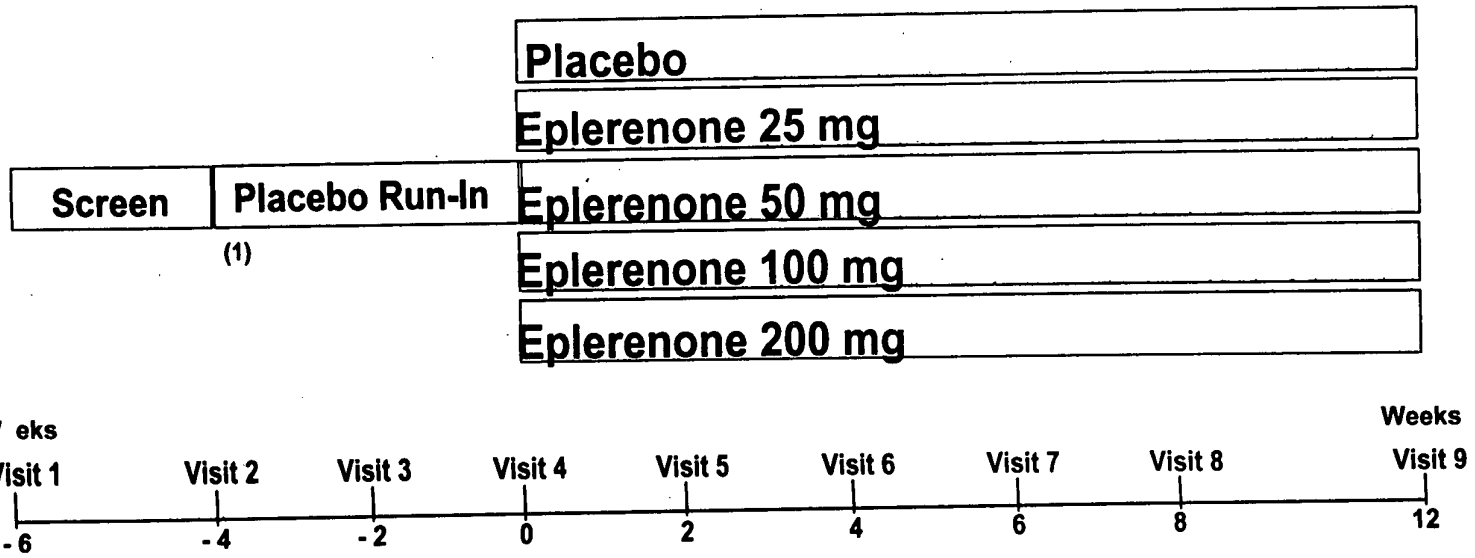
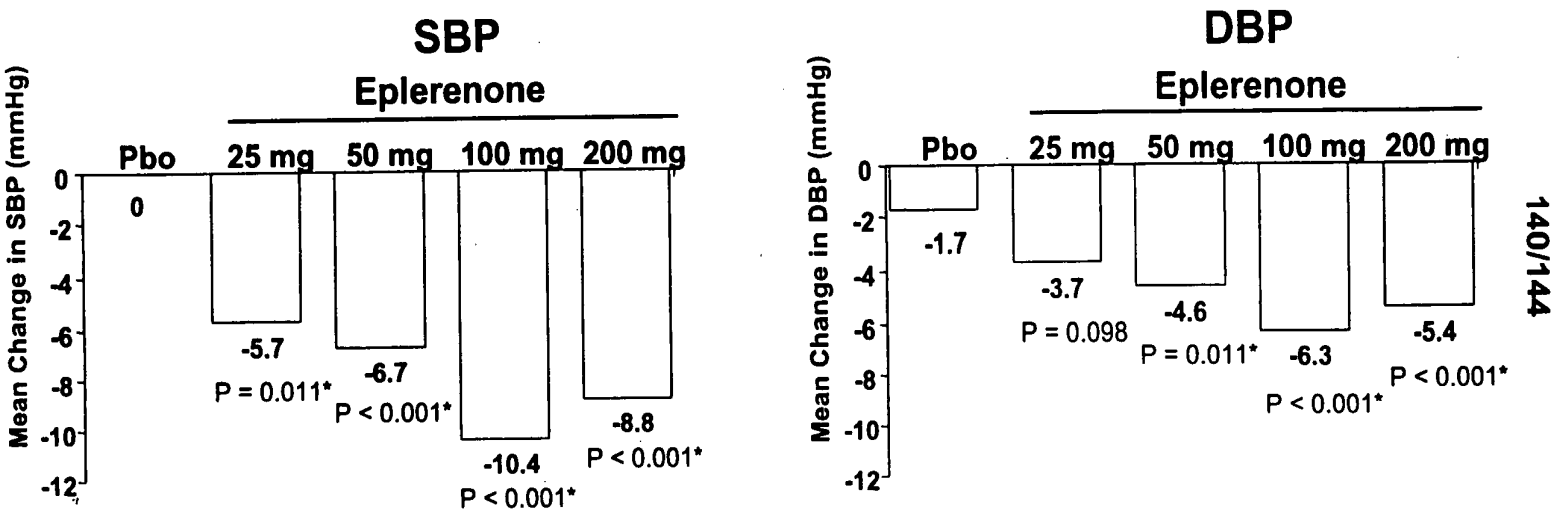
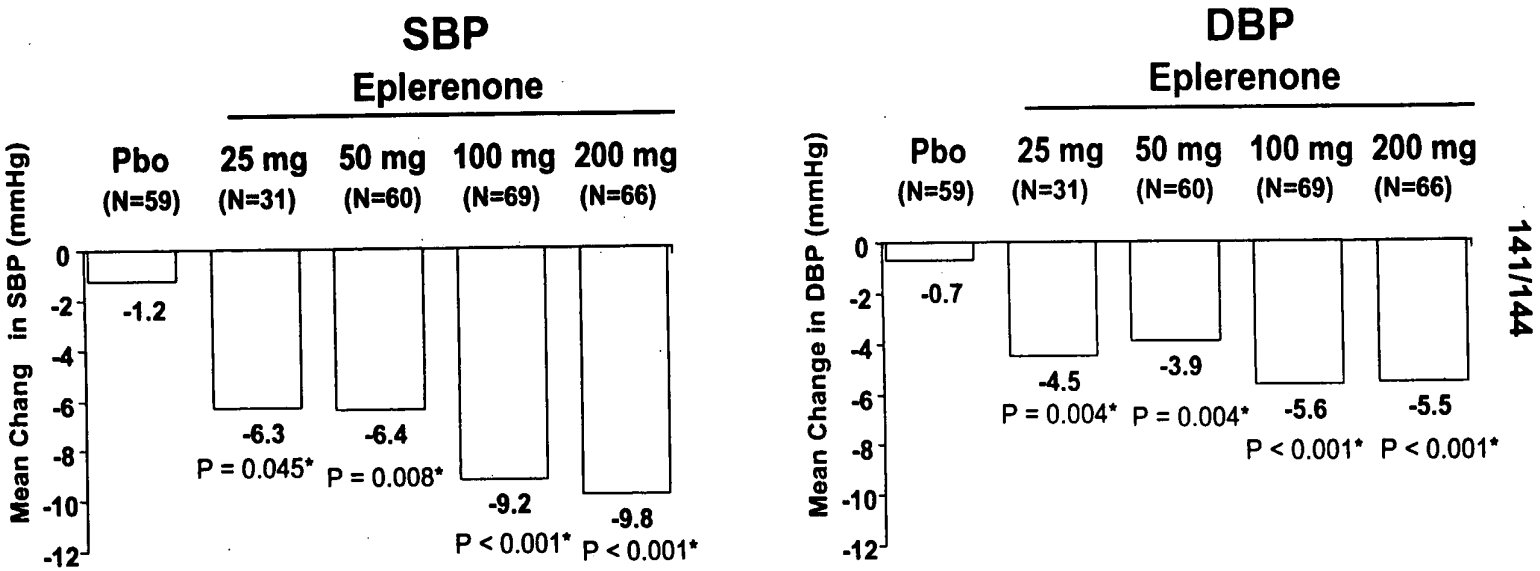


Figure D-74 - Mean Change from Baseline: Cuff BP Week 12 (Final Visit)



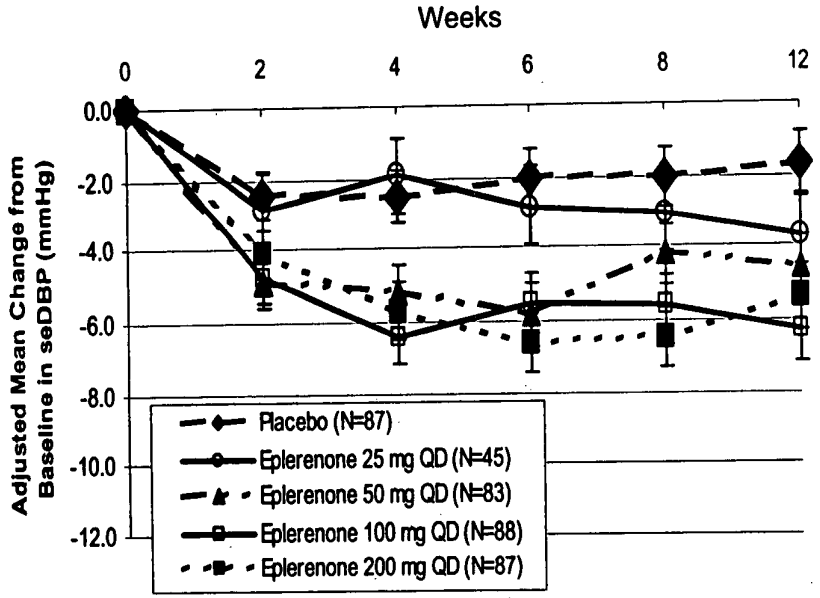
* p-value vs. placebo based on ANCOVA using baseline as covariate and treatment and center as factors

Figure D-75 - Mean Change From Baseline (ABPM)



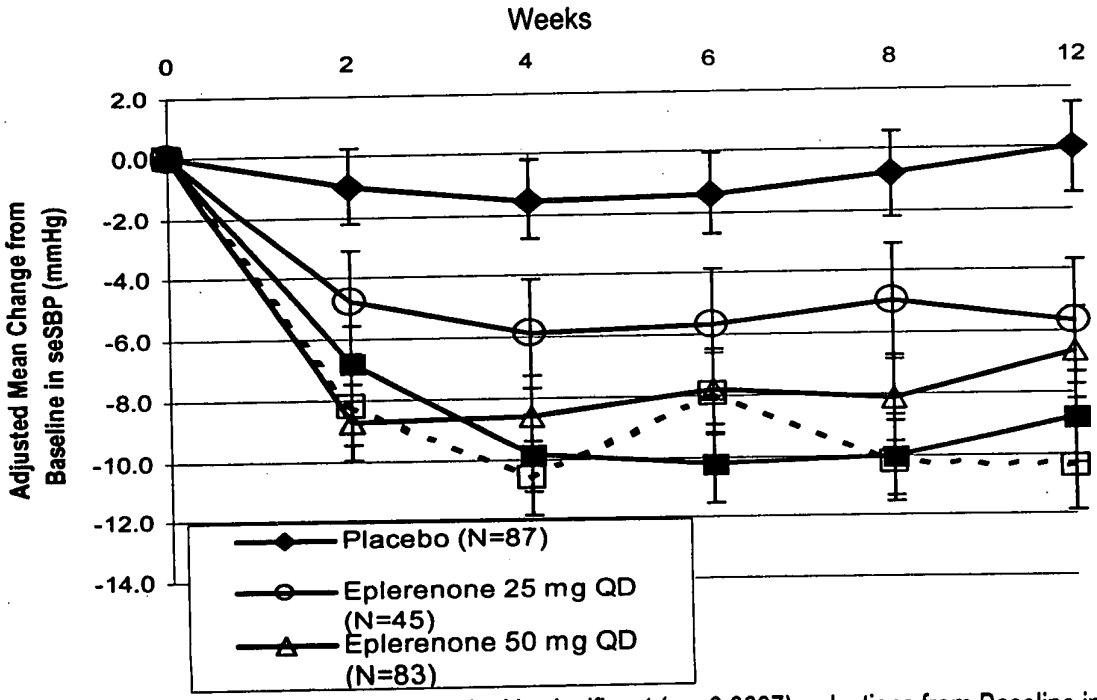
* p-value vs. placebo based on ANCOVA using baseline as covariate and treatment and center as factors

Figure D-76: Eplerenone vs. Placebo Over Time Adjusted Mean Change from Baseline in Cuff seDBP



Note: Eplerenone 50 mg, 100 mg, and 200 mg QD resulted in significant ($p \leq 0.0007$) reductions from Baseline in seSBP at each time point compared to placebo. Eplerenone 25 mg QD resulted in significant ($p \leq 0.0218$) reductions compared to placebo at Weeks 4 and 12.

Figure D-77: Eplerenone vs. Placebo Over Time Adjusted Mean Change from Baseline in Cuff seSBP



Note: Eplerenone 50 mg, 100 mg, and 200 mg QD resulted in significant ($p \leq 0.0007$) reductions from Baseline in seSBP at each time point compared to placebo. Eplerenone 25 mg QD resulted in significant ($p \leq 0.0218$) reductions compared to placebo at Weeks 4 and 12.

Figure D-78 - Events of Special Interest

Adverse Events	Pbo (N = 90)	Eplerenone 25 mg (N = 45)	Eplerenone 50 mg (N = 87)	Eplerenone 100 mg (N = 90)	Eplerenone 200 mg (N = 88)
Aggravated Hypertension	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hyperkalemia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)
Hyperuricemia	1 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)
Increased Lab Values					
GGT	2 (2.2)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
SGOT	1 (1.1)	0 (0.0)	1 (1.1)	1 (1.1)	0 (0.0)
SGPT	1 (1.1)	0 (0.0)	1 (1.1)	2 (2.2)	0 (0.0)
BUN	1 (1.1)	0 (0.0)	2 (2.3)	0 (0.0)	0 (0.0)
Impotence*	1 (1.9)	0 (0.0)	0 (0.0)	1 (2.1)	0 (0.0)
Gynecomastia*	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypotension	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)
Menstrual Irregularities**	1 (2.8)	0 (0.0)	1 (2.6)	1 (2.3)	0 (0.0)

* N=54 (Pbo); 27(25mg); 48(50mg); 47(100mg); 48(200mg)

** N=36 (Pbo); 18(25mg); 39(50mg); 43(100mg); 40(200mg)